Volume 15 No.3 2004

Documents of the NRPB

Review of the Scientific Evidence for Limiting Exposure to Electromagnetic Fields (0–300 GHz)

Headquarters
Chilton, Didcot,
Oxfordshire OX11 0RQ

www.nrpb.org

Working in partnership with the
Health Protection Agency

Contents

Review of the Scientific Evidence for Limiting Exposure to Electromagnetic Fields (0–300 GHz)

REVIEW OF THE SCIENTIFIC EVIDENCE FOR LIMITING EXPOSURE TO ELECTROMAGNETIC FIELDS (0–300 GHz)

ABSTRACT

This document reviews the scientific evidence relating to possible adverse health effects of exposure to electromagnetic fields (EMFs) in the frequency range 0–300 GHz. It provides the basis of NRPB advice on quantitative restrictions on exposure and other measures to avoid adverse effects. It explores recent evidence on the possibility of variations in sensitivity between different groups in the population.

The preparation of this review has been carried out at the request of the Department of Health and has particularly examined the issues of uncertainty in the science and aspects of precaution. In developing this review, NRPB has taken advice from individual UK and international scientific experts, and from published comprehensive reviews by expert groups. It sought advice from an ad hoc expert group on weak electric field effects in the body and gave careful consideration to the views expressed in response to a consultation document on its proposed guidelines issued in May 2003. It has also listened to the concerns raised at a public open meeting on power lines in December 2002.

Having considered the totality of the scientific evidence in the light of uncertainty and the need for a cautious approach, NRPB recommends that restrictions on exposure to EMFs in the UK should be based on the guidelines issued by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) in 1998. This provides for basic restrictions on exposures of members of the public that are a factor of five lower than for those who are occupationally exposed.

PREPARED BY A F McKINLAY, S G ALLEN, R COX, P J DIMBYLOW, S M MANN, C R MUIRHEAD, R D SAUNDERS, Z J SIENKIEWICZ, J W STATHER AND P R WAINWRIGHT

This report from NRPB reflects understanding and evaluation of the current scientific evidence as presented and referenced in this document.

Executive Summary

BACKGROUND

1 The National Radiological Protection Board (NRPB) has the responsibility for providing advice on exposure guidelines for electromagnetic fields (EMFs) in the frequency range from 0 to 300 GHz. In 1993, NRPB published a comprehensive review of epidemiological and experimental data relevant to the assessment of health effects from exposure to EMFs and provided advice on limiting exposure. This advice gave similar exposure guideline values for workers and members of the public. NRPB subsequently reviewed its advice in 1999 following publication of exposure guidelines by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) with restriction values for workers broadly similar to those of NRPB but which also included more restrictive values for members of the public. At the time NRPB saw no scientific evidence for changing its previous advice.

2 Between 1993 and 1999, many studies addressing exposure to EMFs and possible effects on health had been published and NRPB had carried out continuous surveillance of these through scientific reviews carried out by its own staff and through the independent Advisory Group on Non-ionising Radiation (AGNIR), ICNIRP, the World Health Organization (WHO), and expert bodies in other countries. Since 1999, when NRPB last published advice on EMF exposure guidelines, there have been further comprehensive reviews carried out including those from AGNIR, an Independent Expert Group on Mobile Phones (IEGMP), ICNIRP and the International Agency for Research on Cancer (IARC), and other national bodies. During this period the question of scientific uncertainty and its role in the development of EMF exposure guidelines has also been further addressed by NRPB and others.

GUIDELINES – ONGOING DEVELOPMENTS

3 Since 1999, recommendations as to the further development of exposure guidelines and their implementation within the frameworks of national and international policy on EMFs and health have been promulgated by a number of bodies.

4 WHO has launched an initiative aimed at achieving a harmonised international approach to the development of guidelines, a keystone of which is that exposure guidelines should be based on thorough reviews of the science. ICNIRP, NRPB and expert committees in other countries concerned with the development of exposure guidelines have already adopted this approach.

5 The European Commission has urged the need for harmonisation of standards for protection within the European Union (EU). A Recommendation to EU Member States on the limitation of exposure of the general public to EMFs in the frequency range from 0 to 300 GHz was passed on 12 July 1999 by the Council of the European Union and published in the *Official Journal of the European Communities*. In its preamble, the

Recommendation states that 'measures with regard to electromagnetic fields should afford all Community citizens a high level of protection: provisions by Member States in this area should be based on a commonly agreed framework, so as to contribute to ensuring consistency of protection throughout the Community.' The UK supported the Recommendation.

6 In May 2000, IEGMP published a report on mobile phones and health. This report contained a recommendation to government to adopt, 'as a precautionary approach', the general public exposure guidelines of ICNIRP for mobile telephony. The government responded positively to this recommendation and the Board of NRPB supported the government's response. The Board noted that it had foreseen in its statement of 1999 that, in the absence of direct scientific evidence, government may take other factors into account in establishing generally accepted exposure guidelines for the public. Moreover, in issuing the Board's supportive statement it was recognised that the Board's advice would be further developed following detailed consideration of the IEGMP recommendation, taken together with other relevant information. Support for the IEGMP recommendation has additionally been expressed by various other UK bodies in connection with planning issues concerning the development of telecommunications masts. These include the (then) Department of the Environment, Transport and the Regions, the Welsh Assembly Government, the Scottish Executive, and the Department of the Environment for Northern Ireland. Recommendations to adopt parts of the ICNIRP exposure guidelines had also previously been made by the Select Committee on Science and Technology and the Scottish Parliament Transport and the Environment Committee in their reports on mobile telecommunications.

EMFs AND HEALTH

7 This document is a review of the scientific data relating to possible adverse health effects of exposure to EMFs and the conclusions that NRPB draws from these data with respect to providing advice on quantitative exposure restrictions, other measures to avoid such effects and aspects of further precaution.

8 This review covers epidemiological studies as well as experimental biology, volunteer studies and dosimetry. These play important individual and collective roles in identifying possible adverse effects on health and in providing information on the need for, and appropriate levels of, protection. In evaluating the possible risks from exposure to EMFs and the basis for providing guidance on limiting exposure, consideration has been given to uncertainties in the scientific data and a cautious approach has been adopted in their interpretation.

9 NRPB is aware of, and sympathetic to, concerns about EMFs and health expressed by members of the public through both individual and media enquiries to which it responds. NRPB welcomed the positive response from members of the public and others who participated in an open discussion meeting on power lines that it organised at the National Exhibition Centre, Birmingham, in December 2002. It also values the information about issues raised at the open meetings held around the country by IEGMP.

EXPOSURE GUIDELINES

Scientific basis

10 The review of scientific information on possible health effects considers information published since previous NRPB reports in 1993 and 1999. It also takes account of advice from AGNIR and recent reports issued by other expert bodies, including ICNIRP and WHO. The review has covered epidemiological studies as well as experimental biology, volunteer studies and dosimetry. Taken together, these areas of the science play an essential role in identifying possible adverse effects on health and in providing information on appropriate exposure guideline levels.

11 A major difficulty in the development of EMF exposure guidance is that interpretation of studies of potential health effects is controversial. There exists a spectrum of opinion within the scientific community and elsewhere. Recognising this, various national and international expert bodies have undertaken major reviews of the scientific literature, which have, by and large, achieved a wide degree of consensus.

12 This review by NRPB staff examines the scientific evidence taking account of the major reviews and individual studies that address specific issues. NRPB concludes that there are scientific data indicating appropriate quantitative restrictions on exposure. These data derive from experimental studies related to effects of EMFs on the central nervous system and effects of heating on the body. The nature of such effects and the mechanisms underlying them are reviewed in this document. The recommended quantitative restrictions on exposure and also recommendations for further investigation, where relevant, are derived from data on these effects. A cautious approach has been adopted in the interpretation of these scientific data.

13 Evidence of effects associated with EMF exposure, but where the scientific data are insufficient either to make a conclusive judgement on causality or to quantify appropriate exposure restrictions, derives principally from epidemiological studies and from some experimental studies. The main, but not sole, subject of such research has been cancer. These studies have been reviewed extensively by expert groups, including AGNIR, and they are summarised and further reviewed in this document. NRPB concludes that currently the results of these studies on EMFs and health, taken individually or as collectively reviewed by expert groups, are insufficient to derive quantitative restrictions on exposure to EMFs.

14 However, such studies, together with people's concerns, provide a basis for considering the possible need for further precautionary measures in addition to the application of quantitative restrictions on exposure to EMFs.

15 The recommendations in this document are not concerned with exposures of patients carried out under medical supervision or with possible electrical interference with implantable medical devices such as pacemakers. The recommendations do not address detailed aspects of applying the guidelines to specific exposure situations.

16 In the light of ongoing research, NRPB is committed to monitoring the results of scientific studies on EMFs and health and to revising its advice when appropriate.

Scientific uncertainty and caution

17 All scientific investigations are subject to uncertainties, as is the interpretation of the studies relevant to judgements on likely adverse health effects. An example of the latter arises when the results of animal studies are extrapolated to possible effects in people

because of inter-species and inter-strain differences that can exist. Even the results from well-designed and well-conducted epidemiological and experimental studies have uncertainties that can be statistically quantified, but may not always be explained. In addition, not all studies are well designed and executed and this should also be taken into account when assessing the available information.

18 It is necessary therefore, in examining published studies, to identify criteria for assessing the strength of the experimental evidence. The more important criteria in this context are the adequacy of the experimental design, statistical analysis of the data, and the avoidance of possible confounding factors that might otherwise result in a misleading or erroneous conclusion. It is a fundamental principle of scientific investigation that effects described in one laboratory should be repeatable in the same and in other laboratories, provided the correct procedures and protocols are followed. Replication of an effect by an independent laboratory considerably strengthens the view that any effect observed represents a true response and not an experimental artefact, a chance observation, or the result of a systematic error present in the experiment. Major factors in assessing the evidence include: the strength of evidence from an individual experiment; consistency between studies in the same or different laboratories; dose–response relationships; and plausibility and coherence. These factors are consistent with the guidelines formulated by Bradford Hill for the assessment of the strength of epidemiological evidence of adverse health effects.

19 To ensure that exposure guidelines provide general community protection, the health risk assessment includes recommendations based on the above factors and on scientific uncertainties. An intrinsic part of the EMF risk assessment process is the exercise of caution. The degree to which caution is applied in the interpretation of the scientific evidence is a matter of judgement and should be consistent.

20 Generally, occupational exposure concerns healthy adults working under controlled conditions. These conditions include the opportunity to apply engineering and administrative measures and, where necessary and practical, provide personal protection. For members of the public, similar controls do not generally exist and individuals of varying ages have widely varying health status and responses to exposures to EMFs. NRPB judges, on the basis of recent evidence, that the potential for such differences in response needs to be taken into account in recommending exposure guidelines for the public alongside those for workers.

Recommendations for quantitative restrictions

21 The recommendations for quantitative restrictions on EMF exposure set out in this document have been developed by NRPB from this review of the science, whilst noting the advantages of harmonisation of approaches to the development of exposure guidelines as expressed by WHO and the EC.

22 In recommending the quantitative exposure restrictions, judgements have been made as to the degree of uncertainty in the scientific data on the adverse effects on which such restrictions are based and how this indicates the choice of the restriction values. The basic restrictions on exposure recommended in this document for preventing *direct* adverse health effects of exposure to EMFs and other recommendations for limiting the occurrence of *indirect* effects (eg shock and burn) include such considerations and, overall, they reflect a cautious approach.

23 Judgements have also been made concerning the degree to which exposure should be additionally restricted where increased susceptibility is expected on scientific grounds, but where, because there is a lack of specific scientific data, the degree of susceptibility cannot currently be precisely determined. These judgements form the basis of recommendations for more restrictive exposure values for members of the public compared with those for workers.

24 Where the science has pointed to a need for NRPB to revise its extant advice it has done so. However, given the uncertainties in the science, there appears to be neither scientific justification nor, considering harmonisation of approaches to exposure guidelines, any practical merit in recommending new restrictions that are close to those of ICNIRP but differ from them.

25 This approach leads to the recommendation to adopt the ICNIRP exposure guidelines.

26 Further, NRPB noted the advice provided by an ad hoc expert group on effects of weak electric fields and by other experts attending a ICNIRP/WHO workshop on weak electric field effects in the body. As a result, it has concluded that internal electric field strength is the appropriate dosimetric quantity with which to express basic restrictions for low frequency electric and magnetic fields. This judgement and other similar ones based on uncertainties and new scientific data are intended to stimulate scientific discussion towards the future development of EMF exposure guidelines.

ASPECTS OF FURTHER PRECAUTION

27 NRPB generally supports the concepts in the WHO initiative on a 'Precautionary Framework for Public Health Protection'. It considers that, with further development, such a framework can be an effective tool for considering the possible need for precautionary measures in relation to health in general and EMF exposure in particular.

28 The government should consider the need for further precautionary measures in respect of exposure of people to EMFs. In doing so, it should note that the overall evidence for adverse effects of EMFs on health at levels of exposure normally experienced by the general public is weak. The least weak evidence is for the exposure of children to power frequency magnetic fields and childhood leukaemia.

Power frequency fields

29 In the context of possible adverse health effects from EMFs, the conclusions of published expert scientific reviews have identified only one reasonably consistent epidemiological finding of an adverse health outcome associated with exposure to EMFs at levels lower than exposure guidelines: that is an apparent increased risk of childhood leukaemia with time-weighted exposure to power frequency magnetic fields above 0.4 μT. It is the view of NRPB that the epidemiological evidence is currently not strong enough to justify a firm conclusion that such fields cause leukaemia in children.

30 In 2002, IARC classified power frequency magnetic fields as a possible carcinogen.

31 The view of NRPB is that it is important to consider the possible need for further precautionary measures in respect of exposure of children to power frequency magnetic fields.

Radiofrequency fields

32 In 2003, AGNIR examined possible health effects of exposure to radiofrequency (RF) fields, with an emphasis on studies conducted since the IEGMP review in 2000. AGNIR noted that there are many sources of RF fields – at work, at home, and in the environment – but recent emphasis in health-related studies has been on mobile phones and broadcast transmitters.

33 AGNIR also noted that studies reviewed by IEGMP suggested possible cognitive effects of exposure to RF fields from mobile phones, and possible effects of pulse-modulated RF fields on calcium efflux from the nervous system. AGNIR concluded that the overall evidence on cognitive effects remained inconclusive, while the suggestions of effects on calcium efflux had not been supported by more recent, better conducted studies. The biological evidence suggested that RF fields do not cause mutation or initiate or promote tumour formation, and the epidemiological data overall do not suggest causal associations between exposures to RF fields, in particular from mobile phone use, and the risk of cancer. AGNIR noted that exposure levels from living near to mobile phone base stations are extremely low, and concluded that the overall evidence indicates that they are unlikely to pose a risk to health. With respect to possible risks to children's health, AGNIR noted that little has been published specifically on childhood exposures to RF fields and no new substantial studies had been published since the IEGMP report.

34 Overall, AGNIR concluded that, in aggregate, the research published since the IEGMP report does not give cause for concern and that the weight of evidence now available does not suggest that there are adverse health effects from exposures to RF fields below guideline levels. In reaching these conclusions, AGNIR noted that the published research on RF field exposures and health has limitations and mobile phones have only been in widespread use for a relatively short time. The possibility therefore remains open that there could be health effects from exposure to RF fields below guideline levels; hence continued research is needed.

35 From its own review and the advice from AGNIR above, NRPB concludes that the scientific evidence for RF fields causing adverse health effects at levels to which the general public are normally exposed is much weaker than that for power frequency magnetic fields. It also notes there is a great deal of ongoing scientific research on RF fields, in particular mobile telephony, and health. There is a need to constantly monitor the results of this research and keep the guidelines under review.

1 Introduction

BACKGROUND

1 The National Radiological Protection Board (NRPB) has the responsibility for providing advice on limiting exposure to electromagnetic fields (EMFs) in the frequency range from 0 to 300 GHz. In 1993, NRPB published a comprehensive review of epidemiological and experimental data relevant to the assessment of health effects from exposure to EMFs and provided advice on exposure restrictions (NRPB, 1993). This advice gave similar exposure guideline values for workers and members of the public. NRPB subsequently reviewed its advice in 1999 following publication of exposure guidelines by the International Commission on Non-Ionizing Radiation Protection (ICNIRP), which included more restrictive values for the public (ICNIRP, 1998). At the time, NRPB saw no scientific evidence for changing its previous advice.

2 In May 2000, an Independent Expert Group on Mobile Phones published a report on mobile phones and health (IEGMP, 2000). This report contained a recommendation to government to adopt, 'as a precautionary approach', the general public exposure guidelines of ICNIRP for mobile telephony. The government responded positively to this recommendation and the Board of NRPB supported the government's response (NRPB, 2000). The Board noted that it had foreseen in its statement of 1999 that, in the absence of direct scientific evidence, government may take other factors into account in establishing generally accepted exposure guidelines for the public. Moreover, in issuing the Board's supportive statement it was recognised that the Board's advice would be further developed following detailed consideration of the IEGMP recommendation, taken together with other relevant information.

3 The recommendation by IEGMP to adopt the ICNIRP exposure guidelines was put forward 'as a precautionary approach' to reflect some uncertainties in knowledge about possible biological effects of exposures to radiofrequency (RF) fields. A recommendation to adopt the ICNIRP guidelines for RF exposure had already been made by the Select Committee on Science and Technology (SCST, 1999) and supported by the Scottish Parliament Transport and the Environment Committee (SPTEC, 2000) in their respective reports on mobile telecommunications. Support for the IEGMP recommendation has also been expressed by various other UK bodies in connection with planning issues and the development of telecommunications masts. These include the (then) Department of the Environment, Transport and the Regions, the Welsh Assembly Government, the Scottish Executive, and the Department of the Environment for Northern Ireland. Furthermore, the ICNIRP guidelines provide the basis for a Council of the European Union (CEU) Recommendation on limiting exposure of the general public to EMFs (CEU, 1999), which the UK supported. This Recommendation covers the EMF spectrum up to 300 GHz, encompassing static fields and power frequencies (50 Hz in the UK), in addition to RF fields.

4 This document is a review of the scientific data relating to possible adverse health effects of exposure to EMFs and the views that NRPB draws from these data with respect to providing advice on quantitative exposure restrictions, other measures to avoid such effects, and aspects of further precaution.

5 The scientific review covers epidemiological studies as well as experimental biology, volunteer studies and dosimetry. These play important individual and collective roles in identifying possible adverse effects on health and in providing information on the need for, and appropriate levels of, protection. In evaluating the possible risks from exposure to EMFs and providing guidance on limiting exposure, consideration has been given to uncertainties in the scientific data and a cautious approach has been adopted in their interpretation.

6 The recommendations in this document are not concerned with exposures of patients carried out under medical supervision or with possible electrical interference with implantable medical devices such as pacemakers. The recommendations do not address detailed aspects of applying the guidelines to specific exposure situations.

7 NRPB is aware of, and sympathetic to, concerns about EMFs and health expressed by members of the public through both the individual and media enquiries to which it responds. NRPB welcomed the positive response from members of the public and others who participated in an open discussion meeting on power lines that it organised at the National Exhibition Centre, Birmingham, in December 2002. It also values the information about issues raised at the open meetings held around the country by IEGMP.

DEVELOPMENT OF EXPOSURE GUIDELINES

8 National and international guidelines for limiting exposure to EMFs have the objective of preventing adverse effects on health.

9 Guidelines on limiting exposure to EMFs from ICNIRP and NRPB, as well as from various expert bodies in other countries, have been based on thorough reviews of the science. This approach necessitates a measure of caution both with respect to assessing individual studies and their significance in identifying possible adverse effects on human health and with respect to addressing the uncertainties in the science. These bodies have all exercised caution in respect of arriving at judgements on exposure levels for preventing health effects that are supported by the scientific evidence. An important aspect of this approach is the need to highlight where data are sparse and/or inconclusive and to identify where further relevant research is appropriate.

10 Epidemiological and biological data together with dosimetric information underpin the basic framework for exposure restrictions on EMFs and the derivation of external field strength levels used in assessing compliance with the guidelines.

11 IEGMP supported the approach to the analysis of the scientific data by NRPB and concluded 'The balance of evidence to date suggests that exposures to RF radiation below NRPB and ICNIRP guidelines do not cause adverse health effects to the general population' (IEGMP, 2000, paragraph 6.37). However, it decided to adopt 'a precautionary approach' in its recommendations on guidelines for exposure to RF radiation in the light of gaps in scientific knowledge concerning RF exposure and the scientific evidence 'which suggests that there may be biological effects occurring at exposures below these guidelines' but not necessarily effects that could lead to disease (IEGMP, 2000, paragraph 6.38).

12 The IEGMP report identified a number of uncertainties related to exposures to RF fields. IEGMP noted that some information was available that suggested RF fields below guideline levels may have an effect on brain function. There was concern that if there are any unrecognised health risks from mobile phone technology then children would be more likely to be vulnerable. IEGMP also noted that within the general population there may be people with illnesses that render them unusually susceptible to the heating effects of RF fields.

13 There are also uncertainties in relation to the effects of extremely low frequency (ELF) EMFs on the body. The independent Advisory Group on Non-ionising Radiation (AGNIR, 2001a) has reviewed the possibility that ELF EMFs may be implicated in the development of cancer. The conclusions of this and other scientific reports (eg IARC, 2002) are discussed in this current document. In addition, AGNIR has addressed possible effects of power frequency (50/60 Hz) electric fields on diseases of the central nervous system (AGNIR, 2001b). Further uncertainties related to possible effects on the functioning of the central nervous system are also discussed in this document.

14 The principal focus of this document is on establishing guidelines for preventing adverse health effects resulting from direct exposure to EMFs. Where appropriate scientific data are available on effects due to indirect exposure, such as from electrical contact with or discharge from an electrically charged object, these are also considered. Putative effects resulting from the consequences of electric charge on the inhalation of pollutant particles or their deposition on the skin are not considered in detail in this document. AGNIR has considered mechanisms for such effects (AGNIR, 2004).

15 NRPB advice on limiting exposure to EMFs is based on the totality of the scientific evidence and is broadly in line with that from ICNIRP, although some uncertainties remain.

16 NRPB considers it important to address such uncertainties and has therefore carried out a comprehensive review of the science that provides the basis for recommending exposure guidelines. This review is set out in the current document. Consideration is given to the role of a cautious approach to the interpretation of scientific uncertainties and to aspects of further precaution.

17 A significant difference between the UK exposure guidelines on limiting exposure to EMFs and those of ICNIRP – and their derivatives (including the CEU Recommendation for limiting exposure of the general public) – is the distinction between workers and the general public by ICNIRP and the application of further restrictions on exposure for the latter. Hence, in preparing this document, NRPB has set out to address this specific issue, ie whether the more restrictive exposure values for the general public are supported by current scientific knowledge. In order to benefit from additional scientific and medical expertise, NRPB has consulted various external experts.

18 Advice on limiting exposure includes basic restrictions on exposure which, as far as possible, address uncertainties in the scientific data related to adverse health effects. Generally, basic restrictions on exposure are expressed in terms of internal dose quantities, which usually cannot be measured directly.

19 Computational dosimetry provides the quantitative link between internal dose quantities for direct effects and external fields that can be measured. Reference levels are values of external fields that are intended to ensure the basic restrictions are not

exceeded. The dosimetry in this document is based on realistic computational modelling of the human body under conservative exposure conditions.

STRUCTURE OF DOCUMENT

20 In developing this review, NRPB has taken advice from individuals in the UK, international scientific experts, and from published comprehensive reviews by expert groups. It has also taken advice from an ad hoc expert group on weak electric field effects in the body. It has given careful consideration to the views expressed in response to a consultation document issued in May 2003. It has also listened to the concerns raised at a public open meeting on power lines in December 2002.

21 The remainder of the document is set out as follows:

(a) the scientific basis for the development of exposure guidelines (Chapter 2) and specifically the roles of the various scientific and medical disciplines involved,
(b) detailed reviews of the epidemiology, biology and dosimetry of:
  (i) static electric and magnetic fields (Chapter 3),
  (ii) electromagnetic fields of frequencies below 100 kHz (Chapter 4),
  (iii) electromagnetic fields of frequencies above 100 kHz (Chapter 5),
(c) scientific uncertainty (Chapter 6),
(d) conclusions and recommendations (Chapter 7).
(e) advice from the ad hoc expert group on effects of weak electric fields is given in Appendix A, and related, more recent developments in weak field effects follow in Appendix B; the ICNIRP exposure guidelines (ICNIRP, 1998) are summarised in Appendix C,
(f) a glossary of terms.

2 Development of Exposure Guidelines

1 This chapter examines the role of science in the development of guidelines for limiting exposure of people to electromagnetic fields (EMFs) to prevent adverse health effects. Specifically, the role of different medical and scientific disciplines is discussed, including most importantly epidemiology, biology (human, animal and cellular studies), and computational dosimetry.

2 A major difficulty in the development of EMF exposure guidance is that the interpretation of studies of potential health effects is controversial. There exists a spectrum of opinion within the scientific community and elsewhere. Recognising this, various national and international expert bodies have undertaken major reviews of the scientific literature, which have, by and large, achieved a wide degree of consensus.

3 In principle, the results of studies most closely related to the actual exposure of people to EMFs and the physiological and/or adverse health effects that might result from or correlate with such exposures are of greatest importance to the development of exposure guidelines – that is, well-controlled human laboratory and epidemiological studies.

4 Animal studies are also important, as discussed below, but with caveats as to the conclusions that might be drawn from them with respect to effects on human health.

5 Cellular studies can provide data that increase knowledge about possible mechanisms of biological interaction at the cellular and subcellular level in living systems.

6 Computational dosimetry provides both knowledge of the nature of the physical interactions of EMFs with living matter (people, animals and *in vitro* preparations) and knowledge linking the strengths of external fields to which people may be exposed with those of fields induced in their bodies.

7 Experimental dosimetry plays an important complementary role with computational dosimetry, but more with regard to the measurement of people's exposures and assessing compliance with exposure guidelines than with the development of exposure guidelines *per se*.

8 Guidelines for limiting exposure of people to EMFs are intended to provide a framework for a system of protection by recommending limits, generally termed *basic restrictions*, to avoid the adverse health consequences of exposure.

9 Another set of levels, generally termed *reference levels* (or *investigation levels*), is also provided in exposure guidelines. These are expressed as field and electric current quantities in order to assist the assessment of compliance with the basic restrictions for particular exposure situations. NRPB advice has not been prescriptive with regard to setting field limits, in order to allow the health and safety professional to use the most up-to-date measurement and computational techniques in assessing compliance with the basic restrictions. This system, first developed by NRPB (1993), has proved effective in practice and has been adopted by other expert advisory bodies including the International Commission on Non-Ionizing Radiation Protection (ICNIRP, 1998).

EPIDEMIOLOGY

10 Epidemiology can be defined as the study of the distribution of disease in populations and of the factors that influence this distribution. In contrast to clinical medicine where the emphasis is on treating the individual, epidemiology is concerned with evaluating patterns of disease among groups of individuals. Consequently the conclusions drawn from epidemiological studies are applicable generally, rather than to specific individuals.

11 Epidemiology has proved to be of great value in studying the effects of various agents on human health and, particularly for cancer, in quantifying risks (Doll, 1998). However, some caveats should be borne in mind when attempting to interpret epidemiological results, as follows.

Bias and confounding

12 Epidemiology is generally *observational* rather than experimental in nature. In contrast to controlled studies in which subjects are randomised 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 (ie a systematic tendency to error as a consequence of the design or conduct of the study) or confounding (ie spurious findings due to the effect of a variable that is correlated with both the exposure and disease under study). For example, the quality of information on exposures obtained directly from diseased people or their relatives may differ from that obtained from people without the disease; in particular, the recall of past events may differ between the two groups (recall bias). Alternatively, workers exposed to EMFs may also be exposed to another agent in the workplace that could influence their disease risk – for example, welding fumes in the case of welders.

13 Epidemiologists generally attempt to address the above 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.

Statistical power

14 An important aspect of an epidemiological study is its statistical power, ie the probability that it will detect a raised risk of given magnitude with a specific degree of confidence. Statistical power would normally be calculated prior to initiating a study – for example, to evaluate the probability of detecting a doubling of risk, say, using a significance test at the 5% level. Once a study has been conducted, its precision can be gauged by the width of the confidence interval for the estimated effect.

15 There are several ways in which the power of a study can be increased. In a case–control study, in which exposures are compared for people with the disease of interest (cases) and people selected from the same source population who do not have this disease (controls), efforts could be made to increase the numbers of cases and controls. For example, the geographical area or the time period over which the study is to be conducted could be maximised, although there would be practical constraints in doing so. For a cohort study, in which a group of individuals is followed to determine their subsequent disease incidence or mortality, the cohort size or the period of follow-up may be increased, or attention may be focused on a disease with a relatively

high baseline rate. Another possibility would be to widen the range of exposures. However, within a specific locality or workplace, the opportunity to increase power may often be limited; there would be little gain from including large additional numbers of people with little or no exposure. Both the precision and accuracy of epidemiological findings can also be affected by uncertainties in quantifying exposures. In particular, errors in the assessment of individual exposures which are non-differential (ie unrelated to disease) and random tend to reduce statistical power, and to bias estimates of trend in risk with exposure towards zero (Armstrong, 1998). However, such errors can sometimes lead to a spurious increase in risk estimates (Sorahan and Gilthorpe, 1994). Assessment of exposure to EMFs remains a challenge in epidemiological studies, particularly of occupational groups (Kheifets, 1999).

16 In view of the above, attempts are sometimes made to combine results from different studies of the same topic. One approach involves a meta-analysis of published summary measures from various studies. Whilst meta-analyses are often relatively easy to perform, they can sometimes be limited by the degree of data available and by differences in the way in which data from individual studies were collected and analysed. It is often preferable to undertake a combined analysis based on individual level data from each of the available studies (Blettner et al, 1999). Whilst each investigation may be subject to its own particular sources of bias, this approach allows data from the studies to be analysed in parallel and may identify any lack of comparability between the studies. The decision on whether to combine results across studies can then be made in the light of the evidence for inter-study heterogeneity.

Hypothesis testing or hypothesis generating

17 It is important to distinguish epidemiological studies that set out to *test* a specific hypothesis, based on *a priori* evidence that arose elsewhere, from studies that aim to *generate* hypotheses about possible risk factors for which any *a priori* evidence is weak or absent. It is easier to interpret a correlation found between the presence of a factor and the risk of disease if there had been prior reason to think that it might occur. Otherwise, if a range of possible factors is examined without prior preference for any particular one, then one of them might yield a positive finding simply by chance. For example, suppose 20 distinct causes of death were analysed using a statistical test at the 5% level. The probability of a false positive result for any one of these causes would be 1 in 20, and so it would not be at all surprising to have at least 1 positive result among the 20 causes of death owing to chance alone. Consequently, a hypothesis generated in such a way would usually need to be tested in a separate study.

Epidemiological interpretation

18 Epidemiological studies of people exposed to EMFs have the advantage over animal studies of providing direct information on the health of people subject to such exposures. Also, the difficulties of low statistical power and multiple hypothesis testing highlighted in paragraphs 14–17 can affect the interpretation of any study requiring statistical evaluation, and not just epidemiological studies. The observational nature of epidemiology makes it difficult to infer causal relationships based on epidemiological studies alone, and such inferences are possible only when the evidence is strong. Nevertheless, in combination with information from other sources (eg on biological

plausibility), epidemiological studies can assist in testing for causality – for example, using the guidelines suggested by Bradford Hill (1965). Therefore, epidemiological results can provide an input to guidelines for limiting exposure, although the importance of information from other sources – as reviewed in this document – should be recognised. Furthermore, the strengths and weaknesses of both epidemiological and experimental findings require critical review.

19 In view of the size of the literature and because many of the relevant studies have previously been reviewed by various scientific committees, this document largely cites such reviews. However, individual studies are also cited in order to address specific issues (for example, concerning the strengths or limitations of certain types of study), or where such studies have been published after earlier reviews were conducted (for example, recent studies of mobile phone use and cancer). In contrast to the other reviews cited here, a report by the California Department of Health Services Panel (Neutra et al, 2002) involved the use of numerical scales of uncertainty to express judgements that risks might be real. This approach is unlikely, in itself, to provide a more reliable assessment than a non-numerical approach. Of greater relevance to understanding the conclusions reached by the Californian Panel is the lack of emphasis that it placed on experimental findings and its view that certain epidemiological results could not be attributed to chance, bias or confounding. Examples are cited in Chapter 4. paragraphs 8–11 and 15–17.

BIOLOGY

20 In this document, biological studies are taken to include laboratory experiments with volunteers, as well as those with various animal species including rats and mice, and with cultured cells. Exposure may last from a few minutes in the case of volunteer studies, to several years in the case of lifetime animal studies. The main objective of these studies is to determine the sorts of biological responses that occur as a result of exposure to EMFs, and to evaluate any uncertainties concerning the reliability with which these responses can be defined.

21 The studies are further evaluated for the rigour with which they are conducted, their consistency with other experimental results, their biological plausibility and their coherence, or compatibility with current scientific understanding (see paragraph 28). In this context, responses that can be attributed to induced electric fields and currents at low frequencies (up to about 100 kHz) and to heating at higher frequencies are compared with the present understanding of electrophysiological and thermophysiological responses. The distribution of sensitivity within the population, particularly those more susceptible, is identified from this broader literature.

22 Extrapolating from biological effects to possible adverse human health consequences is not straightforward. Biological effects can be defined as any detectable changes in a biological system in response, for example, to EMFs – but not all effects will necessarily result in harm. WHO defines health as the state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity (WHO, 1946). Thus, deciding whether biological changes have adverse health consequences depends on whether they affect the mental, physical or general well-being of exposed people, in

either the short- or the long-term. Permanent damage to organs and tissues is clearly harmful, but transient functional changes are more difficult to categorise. In this regard, the context of the exposure might be important. For example, a transient but marked perception of the field may be entirely inconsequential in most cases, but could be expected to reduce the effectiveness of a worker performing a cognitively demanding task, and be stressful to people chronically exposed.

Human studies

23 Experimental studies using volunteers, including those exposed to EMFs, are restricted for ethical reasons to the investigation of transient physiological phenomena which, in the controlled conditions of a laboratory, can be determined to be harmless. The advantage of volunteer experiments is that they indicate the likely response of other people exposed under similar conditions. Disadvantages of volunteer studies include the innocuous nature of the effects that can be investigated, the often short duration of investigation, and the small number of subjects usually examined. Such experiments are subject to ethical constraints; the subjects are usually adults screened for medical 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 exposure to an agent.

Animal studies

24 Animal studies are frequently based on experiments using inbred strains of mice or rats. The advantage of such studies compared with studies using cells (*in vitro* studies) 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 and behaviour, in a way that cannot always be achieved with cellular studies. Individual animals in inbred strains are genetically identical, thus ensuring a relative consistency of response to the agent in question. Transgenic or gene knockout animal models of certain 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 typically are more expensive and time-consuming. Extrapolation of this information to humans cannot, however, be expected *a priori* to be straightforward since there are obvious differences in physiology and metabolism between species as well as differences in life expectancy, the proliferative capacity of different tissues, DNA repair capacity, and many other variables. However, at a molecular level, there are many similarities between processes in animals and humans. 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 (Balmain and Harris, 2000).

25 Generally, animal studies can be expected to provide qualitative information regarding potential outcomes, but the data would not be extrapolated quantitatively to give reliable estimates of risk (UNSCEAR, 1986), for the reasons outlined above. Quantitative risk estimates applicable to the development of guidance are more properly derived from human studies. However, IARC (2002) noted that, with regard to cancer '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'. Moreover, IARC noted that the possibility that a given agent may cause cancer through a species-specific mechanism that does not operate in humans should be considered.

Cellular studies

26 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* (in animals or people). 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 provided with supplements to enable the cells to grow, and quite often the cell lines used are derived from various types of cancer because of their ability to grow for long periods in culture. AGNIR (2001a) noted that 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 because they are relatively inexpensive and rapid.

Experimental interpretation

27 It is clearly necessary at the outset to identify criteria for assessing the strength of the experimental evidence to be discussed. The more important criteria in this context are the adequacy of experimental design, statistical analysis of the data, and the avoidance of possible confounding that might otherwise result in a misleading or erroneous conclusion (Repacholi and Cardis, 1997). It is a fundamental principle of scientific investigation that effects described in one laboratory can be repeated in the same and in other laboratories, providing the correct procedures and protocols are followed. Thus replication of an effect by an independent laboratory considerably strengthens the view that any effect represents a true response.

28 More general criteria for assessing the strength of evidence from a number of studies for a particular experimental outcome would include:

(a) *strength of evidence* from an individual experiment, which would include the adequacy of the experimental design, the avoidance of potential confounding and the use of appropriate statistical analysis,
(b) *consistency*, which could here include experimental replication as well as similarity of outcome in different experiments,
(c) *dose–response relationship*, the identification of which would clearly strengthen the view that the agent in question was interacting in a systematic way with a biological process,
(d) *plausibility* and *coherence*, by which is meant that the suspected causation is biologically plausible and that it does not seriously conflict with current scientific understanding.

29 These criteria can, of course, only serve as a guide to judgement. On the one hand, failure to comply does not of itself invalidate the outcome but would, in general, indicate a lack of robustness and perhaps warrant further experimental investigation. On the other hand, concurrence with one or more criteria would strengthen the overall weight of the evidence for a particular outcome. Bradford Hill (1965) has formulated similar guidelines for the assessment of the strength of epidemiological evidence for an association between environmental factors and undesirable health effects.

DOSIMETRY

30 Computational dosimetry provides a link between external non-perturbed EMFs and the fields induced within the body. This points to the choice of reference levels in relation to basic restrictions.

31 Computational techniques may also be used to relate specific energy absorption rate (SAR) to temperature rises within the body, thereby helping to indicate basic restrictions on SAR which will avoid adverse heating effects.

32 Maxwell's equations describe the mutual interaction of electric and magnetic fields, and their interaction with materials in time and space. The approach to deriving reference levels is to solve these equations numerically in fine resolution, anatomically realistic models of the body.

Computational modelling of the human body

33 Fine resolution, anatomically realistic models of the body are usually derived from medical imaging data and are referred to as voxel (volume pixel) phantoms. The phantom structure is a three-dimensional array of voxels, each of which has an identifying tag denoting the discrete tissue type or the surrounding air. The main groups working on human dosimetry for EMF exposure guideline development are at NRPB, the University of Utah (USA), the University of Victoria (Canada) and Brooks Air Force Base (USA). A description of their human phantoms is given below.

34 The NRPB male phantom is called NORMAN. A complete description of the acquisition of the medical imaging data and its segmentation into tissue types can be found in Dimbylow (1996, 1997a). The raw MRI data were acquired from a series of continuous partial-body scans of a single subject. The blocks of data were conjoined by rescaling, translation and rotation to form an entire body. The MRI slices were 256 × 256 pixel images in the axial plane. The data volume was rescaled and interpolated to produce cubical voxels with sides of around 2 mm. The 8-bit grey scale images were segmented unambiguously into discrete tissue types. The phantom was normalised to be 1.76 m tall and to have a mass of 73 kg, the values for 'reference man' in ICRP Publication 89 (ICRP, 2002). Hence, the name was derived from NORmalised MAN. The height fixes the vertical voxel dimension, 2.021 mm, and the horizontal dimensions, 2.077 mm, are then fixed by the mass. There are 8.3 million voxels in the body. There were originally 38 different tissues types: skin, fat, muscle, tendon, bone, trabecular bone, blood, brain, spinal cord, cerebrospinal fluid, eye, sclera, humour, lens, oesophagus, stomach wall, stomach contents, duodenum, small intestine, lower large intestine, upper large intestine, pancreas, gall bladder, bile, liver, spleen, kidney, bladder, urine, prostate, testis, male breast, thymus, thyroid, adrenals, heart, lung, air and background domain. An evaluated review of the dielectric properties of all the tissue types in NORMAN was performed by Gabriel (1995) and Gabriel et al (1996a–c). A 4-Cole-Cole dispersion model was fitted to the data for each tissue type to parameterise the conductivity and permittivity as a function of frequency.

35 A phantom developed at the University of Utah (Furse and Gandhi, 1998) was based on MRI scans of a male volunteer of height 1.76 m and mass 64 kg. The MRI scans were taken with a resolution of 3 mm along the height of the body and 1.875 mm for the orthogonal axes in the cross-sectional planes. The mass was thought to be somewhat low for an average man and so the cross-sectional dimensions were increased to 1.974 mm to produce a new mass of 71 kg. In some of their work it was not

possible to run the 1.974 × 1.974 × 3.0 mm resolution model of the whole body and so 3 × 3 × 2 voxels were combined (taking the dominant tissue in each group) to obtain a coarser 5.922 × 5.922 × 6.0 mm model. The MRI sections were converted to images involving 31 tissue types: fat, muscle, bone, compact bone, cartilage, skin, brain, spinal cord, nerve, cerebrospinal fluid, intestine, spleen, pancreas, blood, heart, parotid gland, eye humour, eye sclera, eye lens, liver, kidney, lung, bladder, stomach, ligament, testes, spermatic cord, prostate gland, erectile tissue, pituitary and pineal gland.

36 A phantom used at the University of Victoria (Dawson et al, 1997) was developed from a head and torso model from the Yale Medical School (Zubal et al, 1994). The body model was completed by attaching legs and arms to the Yale model based on representations obtained by applying segmentation algorithms to CT and MRI data from the Visible Human Project at the US National Library of Medicine. The limb dimensions were scaled to match the torso, and additional manual editing was done in the planes of attachment. The height of the final model was 1.77 m with an estimated mass of 76 kg. The original model resolution is 3.6 mm. A 3 × 3 × 3 median filtering algorithm was applied to this model to develop a lower resolution model composed of 7.2 mm cubic voxels. This phantom will be referred to as the UVic phantom in this document.

37 The Brooks Digital Anatomical Man (Mason et al, 1999) was based on photographic data from the Visible Human Project created by the National Library of Medicine and the University of Colorado Health Sciences Center. A segmented dataset based on the photographic images was created by a collaboration between the National University of Singapore and Johns Hopkins University. Each of the 1878 axial slices was coded by hand into a palette of colours that represented 39 tissue types. The initial anatomical dataset was at a resolution of 1 mm but this was rescaled to 3 mm to perform SAR calculations.

The development of EMF exposure guidelines builds upon comprehensive reviews of the scientific evidence relevant to possible adverse health effects in people.

Epidemiological studies provide evidence most closely related to the exposure of people to EMFs and the adverse health effects that might result from or correlate with such exposures. It is difficult to infer causal relationships based on epidemiological studies alone, but such inferences are possible when the evidence is strong. In combination with information from other sources (eg on biological plausibility), epidemiological studies can assist in testing for causality. Epidemiological results therefore provide an input to guidelines for limiting exposure and, as with experimental studies, the strengths and weaknesses of these findings require critical review.

Laboratory volunteer studies provide useful information when well controlled, but are restricted in terms of the endpoints that can be examined and the exposures that can be used.

Experimental studies on animals are important, with reservations as to the conclusions that might be drawn with respect to possible effects on human health.

Cellular studies can provide an understanding of possible mechanisms of biological interaction.

Computational dosimetry provides information on the physical interactions of EMFs with people and quantitatively links the strength of external fields with those fields induced in their bodies.

3 Static Electric and Magnetic Fields

1 In this chapter scientific data relevant to the development of exposure guidelines for static electric and magnetic fields are addressed. Specifically, epidemiological studies, biological studies and physical interactions are reviewed.

EPIDEMIOLOGY

2 Epidemiological studies have focused on workers exposed to static magnetic fields of up to a few millitesla (mT), and the children of such workers. IARC (2002) has reviewed studies of cancer among such workers. In general, these studies have not pointed towards elevated cancer risks, although the number of studies was limited, the numbers of cancer cases were often small, and there was a paucity of information on individual exposure levels. Perhaps the most detailed study was conducted by Ronneberg et al (1999), who used job-exposure matrices to estimate exposures in cohorts of workers at an aluminium smelter. No association was found between the risk of brain cancer or cancers of lymphatic and haematopoietic tissue and either static or power frequency (50/60 Hz) magnetic fields. However, the numbers of cases at the higher exposure levels were small (Ronneberg et al, 1999).

3 There is little information on other health outcomes among workers exposed to static fields. A small study showed no association between the occurrence of sick leave caused by musculoskeletal disorders and exposure to static or power frequency magnetic fields at an aluminium plant, although the data were limited (Moen et al, 1996). However, there is anecdotal evidence unsupported by epidemiology that in conditions of low humidity the associated static electric fields arising from work with visual display units (VDUs) may aggravate existing skin problems and the strain of the actual work may give rise to skin problems among those with a predisposition to them (AGNIR, 1994).

4 Previously, NRPB (1993) noted that only a few studies of groups with occupational exposure to static magnetic fields had been performed. Measurements of field levels were generally not available; an exception is a study of workers at a chloralkali plant exposed to fields of up to 30 mT for whom no increased cancer risk was found, although the number of workers was small (Barregard et al, 1985). Some studies have examined reproductive outcome for workers involved in the aluminium industry or in magnetic resonance imaging (MRI). Mur et al (1998) and Kanal et al (1993) did not find decreased fertility for either male or female workers, respectively. Irgens et al (1999) reported a decreased proportion of males among the offspring of aluminium workers, particularly women, although the potential impact of occupational exposures other than magnetic fields was unclear. In contrast, Kanal et al (1993) found no clear association between work in MRI by females and the gender of offspring, premature delivery, low birth weight or spontaneous abortion, although the low response rate in this study severely limited inferences.

Epidemiological uncertainties

5 The studies cited above have predominantly been of exposures of up to a few tens of mT. No studies of high quality have been carried out of workers occupationally exposed to fields greater than 1 T.

Summary

6 Studies of workers exposed to static magnetic fields up to several tens of millitesla do not overall demonstrate raised health risks. However, the number of studies, their size and the information on exposure levels are generally limited. There is some suggestion that static electric fields associated with work with VDUs may aggravate existing skin conditions.

BIOLOGY

7 Static electric and magnetic fields exist as natural phenomena. Static electric fields develop through the accumulation of electric charges on the surface of objects – for example, on clouds where the electric potential differences may exceed the dielectric breakdown threshold of air resulting in lightning discharges. Typical values range between 500 and 1200 $kV\,m^{-1}$ but may be lower in certain circumstances (Weast, 1980). A static magnetic field of around 20–70 μT exists over the surface of the Earth and is implicated in the orientation and migratory behaviour of certain animal species.

8 There has been a fragmentary and incoherent approach to investigating the biological consequences of exposure to static electric or magnetic fields, and in many areas the data are insufficient to draw conclusions regarding the possibility of health effects, especially following chronic exposure. Although the effects of static magnetic fields have been investigated to a much greater extent than those of static electric fields, this database is not exhaustive. The earlier literature has been summarised by WHO (1987), Kowalczuk et al (1991) and ICNIRP (1994, 1997), while more recent studies have been reviewed by Repacholi and Greenebaum (1999), IARC (2002) and ICNIRP (2004).

9 It is clear that for exposure to static electric fields the major consequences result from perception of the field and from spark discharges induced by touching objects at a different electric potential. The major consequences of exposure to static magnetic fields result from the effects of the electric fields induced in living tissues by movement within the field. These acute effects depend on the magnitude of the respective field, and these will be negligible at levels usually experienced by members of the public. This chapter presents a summary of the studies that have investigated biological effects of static fields in humans, and using animals and cells.

Human studies

Electric fields

10 Static electric fields interact directly with the body by inducing a surface electric charge. Indirect effects can also occur when a person is in contact with a charged conducting object, eg a car exposed to a static field. At sufficiently high voltage the air will ionise and become capable of conducting an electric current between the charged body and a person in good electrical contact with the ground. A charged insulated person touching a grounded object would receive a microshock (spark discharge).

These effects may be painful. However, the threshold static electric field values for such perception will vary depending on the degree of insulation and other factors. Overall, the results of the few studies that have investigated the effects of static electric fields in humans do not suggest exposure is associated with significant health effects (IARC, 2002).

11 Clairmont et al (1989) exposed volunteers to static electric fields up to 40 kV m^{-1} and reported a threshold for perception of around 20 kV m^{-1}. This was possibly associated with corona discharge on the tips of hair shafts. Annoying sensations were induced above about 25 kV m^{-1}.

Magnetic fields

12 Ueno and Iwasaka (1999) and ICNIRP (2004) have reviewed the interactions of static magnetic fields with biological materials. These interactions include magneto-mechanical effects, effects on electronic spin states in certain types of charge transfer processes, and electrodynamic interactions with ionic conduction currents. Ionic currents interact with static magnetic fields as a result of the Lorentz forces exerted on moving charge carriers. This electrodynamic interaction gives rise to an induced electric field. An example of such a process is the induction of electric potentials as a result of blood flow in the presence of a static magnetic field.

13 Prior to the development of MRI techniques, few studies of the effects of static magnetic fields on volunteers had been documented (see WHO, 1987), although various anecdotal reports from laboratories using large particle accelerators existed. However, with the advent of superconducting magnet technology, volunteers could be routinely exposed to static fields of around 1.5 T or more. Most of the acute effects that have been reported are consistent with known mechanisms of interaction.

14 Schenck et al (1992) reported 'dose-dependent' sensations of vertigo, nausea and a metallic taste in the mouth in volunteers exposed to static magnetic fields of 1.5 or 4 T in an MRI system. These occurred only during movement of the head. In addition, magnetic phosphenes could sometimes be seen during eye movement in a field of at least 2 T. These effects are probably attributable to the current induced by movement within a static field, since vertigo and phosphenes can be induced by weak electric currents directly applied to the head (eg Adrian, 1977). However, no damage to the acoustic or vestibular systems were reported by Winther et al (1999) following exposure of healthy volunteers to 2–7 mT for 9 hours.

15 Lorentz forces resulting from the movement of charged particles in a magnetic field will be exerted on ions flowing through nerve membranes in a static field. These could affect nerve function, although they are unlikely to be of biological significance until very large fields (around 20 T) are experienced (Tenforde, 1992). A lack of effect on cognitive performance of volunteers, evaluated using a battery of tasks following exposure to a static magnetic field of 8 T for 1 hour, was reported by Kangarlu et al (1999). An earlier study of a large number of volunteers also reported a lack of effect of MRI exposure involving static magnetic fields of 0.15 T on cognition (Sweetland et al, 1987), although anxiety was increased in the exposed group.

16 Kinouchi et al (1996) noted that the Lorentz force exerted on blood flow generates an electric potential across blood vessels. In practice, so-called 'flow' potentials are readily demonstrated in volunteers exposed to static fields greater than around 0.1 T. Generally, the largest flow potentials occur across the aorta after ventricular contraction

and appear superimposed on the T-wave of the electrocardiogram (ECG) (Tenforde, 1992). The latter indicates the repolarisation of ventricular heart muscle when electrical excitability gradually recovers following contraction (Antoni, 1998). Fibrillation of the heart – potentially fatal asynchronous and irregular cardiac muscle contraction – can be induced only during this 'vulnerable' period. However, the fibrillation threshold is about 10–20 times higher than that for cardiac muscle stimulation *per se*; the latter occurs during diastole, when cardiac muscle is relaxed. Reilly (1998) estimated the first and fiftieth percentile ranks for cardiac stimulation in humans due to induced electric fields to be 5 and 10 V m^{-1}, respectively.

17 Kinouchi et al (1996) calculated that a static field of around 5 T would induce maximum current densities around the sino-atrial node of the heart of about 100 mA m^{-2} (approximately 500 mV m^{-1} using a general tissue conductivity of 0.2 S m^{-1}), which is below the cardiac excitation threshold. In addition, a 5 and 10% reduction in blood flow in the aorta was predicted to occur in static fields of 10 and 15 T, respectively, due to magneto-hydrodynamic interactions. However, Kangarlu et al (1999) found that volunteers exposed to an 8 T field for 1 hour showed no change in heart rate or diastolic or systolic blood pressure either during or after exposure. The ECG recorded during exposure was regarded as uninterpretable due to the superposition of the potential generated by aortic blood flow and smaller potentials generated by blood flow in other vessels. In addition, vertigo and other sensations were recorded during movement in this field.

18 More detailed studies by the same group have recently been published (Chakeres et al, 2003a,b); both were approved by the US FDA Investigational Review Board. The authors reported that exposure of 25 healthy volunteers, aged between 18 and 65 years, to 8 T static fields (duration unspecified) had no effect on cognitive function assessed during exposure using seven standard neuropsychological tests (Chakeres et al, 2003a). The second paper reported a lack of clinically significant effects of exposure to fields of up to 8 T on heart rate, respiratory rate, systolic and diastolic blood pressure, finger pulse oxygenation levels, and core body temperature (Chakeres et al, 2003b). There was a statistically significant trend for systolic pressure to increase with magnetic flux density, but at 8 T this was only 3.6 mm Hg, approximately one-half of the difference seen in moving from a sitting to a supine body position. In order to avoid the transient, movement-induced sensations described above (Schenck et al, 1992), the volunteers were moved very slowly (one or two feet over a few seconds, followed by a 15–30 seconds pause, taking overall about 3–4 minutes) to move into the magnet bore. Nevertheless, nine subjects reported sensations of dizziness, and two reported a metallic taste, assumed to be due to electrolysis of metallic chemicals in the subjects' teeth fillings.

19 One study has examined the effects of exposure to static magnetic fields on melatonin rhythms in male volunteers. Haugsdal et al (2001) reported that a single, nocturnal exposure to a static field of 2–7 mT had no effect on the excretion of 6-hydroxymelatonin sulphate, the major urinary metabolite of melatonin.

Summary

20 For static electric fields, a threshold for perception was reported at around 20 kV m^{-1}, and annoying sensations were induced above about 25 kV m^{-1}. Painful spark discharges can be expected when a person who is well insulated from ground touches a grounded

object, or when a grounded person touches a conductive object that is well insulated from ground; however, the threshold static electric field values will vary depending on the degree of insulation and other factors.

21 Vertigo, nausea, a metallic taste and phosphenes can be induced during movement in static magnetic fields larger than about 2 T. In addition, flow potentials induced in a magnetic field of this value have been calculated to generate electric fields near the sino-atrial node of the heart of about 200 mV m^{-1} during the relative refractory period of the cardiac cycle, when cardiac excitability is relatively low.

Animal and cellular studies

Electric fields

22 Few recent studies have investigated the biological effects of exposure to static electric fields. Rats showed aversive behaviour in an electric field of 55 kV m^{-1} but not to fields of less than 42.5 kV m^{-1} (Creim et al, 1993), although exposure to 75 kV m^{-1} did not induce taste aversion learning (Creim et al, 1995). Results of earlier studies suggest rodent behaviours are not significantly modified by exposure to up to 12 kV m^{-1} (Möse and Fischer, 1970; Bailey and Charry, 1986). No adverse effects on haematology or on reproduction and prenatal and postnatal survival were reported following exposure of mice to fields up to 340 kV m^{-1} (Fam, 1981).

23 IARC (2002) noted that there was insufficient evidence to determine the carcinogenicity of static electric fields.

Magnetic fields

24 The biological consequences of exposure to static magnetic fields have been investigated from a variety of endpoints including effects on cancer, reproduction and development, and on the nervous system. There are only isolated reports of field dependent effects using unique exposure conditions, which makes it impossible to judge the likelihood and generality of any potential health effect.

Cancer

25 There has been some concern that exposure to static magnetic fields may increase the risk of cancer. However, most studies have been performed *in vitro* and have examined effects on cellular processes which, if they malfunction, could contribute to the development of cancer. While of scientific interest, such changes cannot be used alone as evidence of effects *in vivo*. Very few cancer studies *per se* have been carried out with the aim of investigating a direct transformation of normal cells into cancer cells.

26 There is no convincing evidence that static magnetic fields are genotoxic (ICNIRP, 2004). No effects on DNA damage were reported in four strains of *Salmonella* or *E coli* exposed at up to 5 T (Ikehata et al, 1999) or on *E coli* strains disabled for DNA repair exposed at 3 T (Mahdi et al, 1994). Although a co-mutagenic role was suggested by Ikehata et al (1999) using *E coli* exposed to various chemical mutagens, this result was not supported by Schreiber et al (2001) using wild-type *Salmonella* bacteria. Exposure to fields of up to about 1 T did not affect dominant lethal frequency in male germ cells *in vivo* (Mahlum et al, 1979), nor the frequency of chromosomal aberrations and sister chromatid exchanges in cells exposed *in vivo* or *in vitro* (Wolff et al, 1980; Cooke and Morris, 1981; Schwartz and Crooks, 1982; Geard et al, 1984). However, Suzuki et al (2001) reported a dose-dependent increase in the frequency of micronuclei in

mouse bone marrow cells exposed at 3 or 4.7 T, whereas Okonogi et al (1996) reported exposure of Chinese hamster CHL/IU cells at 4.7 T for 6 hours significantly decreased the frequency of micronuclei induced by mitomycin c.

27 A lack of evidence for mutagenicity suggests that exposure is not capable of initiating carcinogenesis. Tumour progression and, by implication, tumour promotion seem to be unaffected by exposure to static fields of at least 1 T (Bellossi and Toujas, 1982; Bellossi, 1984, 1986). Mevissen et al (1993) reported that exposure to a magnetic field of 15 mT for 13 weeks did not significantly affect the incidence of chemically induced mammary tumours, nor did it affect the number of tumours per animal compared with controls; weight per tumour was, however, significantly increased.

28 Effects of static magnetic fields on cell growth and proliferation have been carried out using a mixture of *in vitro* models. No consistent field dependent effects have been observed using fields of up to 1.5 T (Hiraoka et al, 1992; Linder-Aronson and Lindskog, 1995; Wiskirchen et al, 1999, 2000; Buemi et al, 2001), although acute exposure at 200 mT decreased incorporation of [^{3}H]thymidine into the DNA of MCF-7 human breast cancer cells (Pacini et al, 1999b) and exposure to 7 or 8 T for several days was reported to induce large inhibitions in growth in various human cancer cells (Raylman et al, 1996; Oguie-Ikeda et al, 2001). Sabo et al (2002) reported that the metabolic activity of HL-60 cells was reduced by exposure to a 1 T field. In other studies, exposure to 500 mT modified *in vitro* expression of activation markers and interleukin release from human peripheral blood mononuclear cells (Salerno et al, 1999) and immune function was reduced in mouse macrophages and lymphocytes exposed to fields of 25–150 mT for 24 hours (Flipo et al, 1998).

29 Other studies have investigated potential effects on apoptosis using a variety of cell lines, exposure conditions and measures of apoptosis. No field dependent effects were reported by Reipert et al (1997), Narita et al (1997) or Fanelli et al (1999), although the last suggested that magnetic fields may have an inhibitory effect on chemically induced apoptosis in cell lines in which calcium influx has an anti-apoptotic effect. In contrast, Blumenthal et al (1997) and Flipo et al (1998) reported that exposure to static magnetic fields can increase apoptosis.

30 There is little experimental information describing possible effects of chronic exposure. So far, no long-term adverse effects have become apparent. Exposure to fields of up to 2 T had no effect on circulating stress hormone levels (Battocletti et al, 1981), haematological profile (Kelman et al, 1983; Osbakken et al, 1986), or on the few immunological responses investigated (Bellossi, 1983; Kelman et al, 1983; Tenforde and Shrifrine, 1984). Studies by Jankovic et al (1991, 1993a,b, 1994) with rats suggest that the field from an implanted magnet may increase immune competence or reverse reductions in immune function induced by lesions of the locus ceruleus or pinealectomy.

31 Overall, IARC (2002) concluded that there was insufficient evidence to determine the carcinogenicity of static magnetic fields.

Reproduction and development

32 The possibility that static magnetic fields may affect reproduction and development has been examined by several researchers. No consistent field dependent effects have been seen using mammalian species (Kowalczuk et al, 1991; ICNIRP, 2004). Narra et al (1996) reported slight changes in spermatogenesis and embryogenesis in mice

exposed at 1.5 T for 30 minutes, whereas Tablado et al (1996, 1998, 2000) reported that maturation of sperm movement in mice as well as postnatal testicular and epididymus development was unaffected by either single, short-term exposure or continuous, long-term exposure at 0.7 T.

33 Several studies have indicated that implantation and prenatal and postnatal development of the embryo and fetus are not affected by continuous or discrete exposure during gestation to fields from 1 to 9.4 T (Sikov et al, 1979; Konermann and Monig, 1986; Murakami et al, 1992; High et al, 2000). However, Mevissen et al (1994) reported continuous exposure to a 30 mT field slightly decreased the numbers of viable fetuses per litter. As a probable consequence of these smaller litter sizes, prenatal development as measured by skeletal ossification was accelerated, and postnatal growth up to day 50 was increased. There was no effect on postnatal behaviour. Inconsistent increases in the development of the pineal gland in chick embryos were observed by Jove et al (1999) using fields of 18 and 36 mT.

34 Other studies have used MRI fields, which include exposure to intense static fields usually in the range of 1 to 4 T. Field effects have been reported in mice on fetal growth and testicular development (Carnes and Magin, 1996) and on craniofacial size and crown-rump length (Tyndall, 1993). Acute exposure was reported not to affect early mouse embryo development *in vitro* (Chew et al, 2001). MRI fields do not appear to increase the teratogenicity of x-ray induced eye malformations (Tyndall, 1990), although exposure to MRI fields in combination with acute exposure to ultrasound has been reported to reduce fetal size and weight (Magin et al 2000) but this may have been due to stresses associated with the experimental procedure.

35 A few studies have also investigated effects of static magnetic fields on embryo development using non-mammalian species. Irreversible changes were reported in developing chick cerebellum by acute or continuous exposure to a 20 mT field (Espinar et al, 1997). Similarly, exposure to fields of 30 mT (but not 15 mT) delayed the onset of mitosis and increased exogastrulation (gut evagination) in early sea urchin embryos (Levin and Ernst, 1997). Inhibition of growth and vitality of amoeba exposed to 71 or 106 mT have also been reported (Berk et al, 1997). However, exposure to 8 T did not affect early embryonic development of *Xenopus* toads (Ueno et al, 1994a). No effects were reported on early chick development following acute exposure to MRI fields (Yip et al, 1994a,b).

Neurobehavioural effects

36 A number of studies have investigated the effects of exposure to static magnetic fields on the functions of the nervous system and on behaviour. Such investigations can provide a sensitive measure of the physiological effects induced by exposure to the field.

37 The evidence from carefully conducted experiments with rodents is that circadian rhythms (Tenforde et al, 1987) and spontaneous and some learned behaviours (Davis et al, 1984) are unaffected by chronic exposure at about 1.5 T. This result is consistent with a lack of effect of exposure up to about 2 T on isolated nerve preparations (Schwartz, 1978, 1979; Gaffey and Tenforde, 1983) and of exposure to 1.5 T on the electro-retinogram response of cats and squirrel monkeys (Tenforde et al, 1985). However, Levine and Bluni (1994) reported that exposure of Harvest mice to a 300 mT field for 30 minutes impaired subsequent performance in a left–right discrimination task.

38 Using sensitive patch-clamp methods, no changes in resting membrane potential were observed in neuroblastoma cells following brief exposures up to 7.5 mT (Sonnier et al, 2000), although Rosen (1996) reported subtle changes in calcium ion channel activation in GH3 cells exposed at 120 mT and Wieraszko (2000) reported changes in the population spike recorded from rat hippocampal slices exposed to fields of 2–3 mT for 20 minutes. Morphological and molecular changes were reported by Pacini et al (1999a) in cultured human neural cells (FNC-B4) exposed for 15 minutes to a 200 mT field. DNA stability was unaffected.

39 The experimental evidence for an effect of static magnetic fields above 2 T on the nervous system of animals is equivocal. Using behaviour in a T-maze to evaluate aversion, Weiss et al (1992) reported that a field of 4 T (but not 1.5 T) was aversive to rats. Two studies (Thach, 1968; de Lorge, 1979) reported that the performance of learned tasks by squirrel monkeys was reduced during exposure to static fields in excess of about 5 T. Changes in the electrical activity recorded from the brains of squirrel monkeys during exposure to between 2 and 9 T were reported in one study (Biescher and Knepton, 1966), although it has been suggested (WHO, 1987) that these responses could be artefacts, possibly due to muscle activity. A temporary increase in sinus arrhythmia and a decrease in heart rate were observed (Beischer and Knepton, 1964) in squirrel monkeys during acute exposure to magnetic fields between 4 and 7 T, although a threshold could not be identified. Exposure to 5 T fields for 48 hours has also been reported to significantly inhibit food and water intake in mice (Tsuji et al, 1996). Nolte et al (1998) reported that exposure to 9.4 T for 30 minutes could be used as a stimulus to induce conditioned taste aversion in rats.

40 Small increases in the permeability of the blood–brain barrier were reported by Prato et al (1994) following acute exposure of rats to fields of 1.5 or 1.9 T. Similar changes were observed using conventional MRI fields, although manipulation of the radiofrequency field and time-varying magnetic field gradient was able to reverse the observed effect.

41 A number of studies suggest manipulation of the ambient static magnetic field may disturb the normal melatonin rhythm in rodents (see reviews by Kowalczuk et al, 1991, and Reiter, 1993). In these studies, night-time inversion or changes in the orientation of the field at magnetic flux densities approximately equivalent to that of the Earth's magnetic field produced changes in melatonin content in the pineal gland or in enzymes involved in the metabolism of melatonin – weaker or stronger fields, or day-time exposure, had lesser or no effects. Kroeker et al (1996) reported that neither acute exposure at 7 T nor medium-term exposure at 80 mT had any effect on nocturnal pineal or serum melatonin levels in rats. Such phenomena may be linked to the neurobiology of magnetic field detection utilised in homing and migratory behaviour (Schneider et al, 1994; see also ICNIRP, 2004, for a review of avian navigation and magneto-reception in animals). Although melatonin has also been implicated in the physiology of seasonal reproduction (Reiter, 1980) and in cancer (Stevens, 1987, 1994; see Chapter 4, paragraphs 49–78), these possibilities seem less likely to be of relevance here.

Cardiovascular effects

42 Experiments with mammals, including two primate species exposed to fields of less than about 2 T, confirm a lack of effect on cardiac function (Gaffey and Tenforde, 1979,

1981; Gaffey et al, 1980). In particular, there were no significant changes in heart rate or arterial blood pressure in monkeys exposed to 1.5 T, although this exposure was sufficient to generate measurable electric potentials arising from blood flow (Tenforde et al, 1983).

43 The effects of static fields on localised blood flow have been investigated in several studies. Small but significant decreases in microcirculation in the skin and concomitant changes in local and rectal temperature were reported in anaesthetised rats during acute whole-body exposure to fields of around 8 T (Ichioka et al, 1998, 2000). Similarly, changes in blood flow and vasomotor tone have been reported in the ears of rabbits with acute exposure at 1–10 mT (Ohkubo and Xu, 1997; Okano et al, 1999; Okano and Ohkubo, 2001), acute exposure at 250 mT (Gmitrov et al, 2002), or subchronic exposure at 180 mT (Xu et al, 1998). Static fields of about 300 mT applied to the region of the sinocarotid artery in rabbits have also been reported to affect the control of blood pressure and increase baroreflex sensitivity (Gmitrov and Ohkubo, 2002a,b). The mechanism for these effects has not been identified.

In vitro effects of very intense fields

44 Several laboratories have investigated the effects of very intense fields *in vitro*. In particular, Ueno and colleagues have reported various changes in the properties of biological and other materials exposed to 8 T or more, often producing field gradients of about 50 T m^{-1}. These include effects on the flow and distribution of water in small containers (Ueno and Iwasaka, 1994a,b), changes in the behaviour of dissolved oxygen molecules (Ueno et al, 1994b), effects on fibrin (Iwasaka et al, 1994, 1998), changes in the orientation of human erythrocytes (Suda and Ueno, 1999) and osteoblasts (Kotani et al, 2000), increased aggregation of rabbit blood platelets (Iwasaka et al, 2000), and decreases in the activity of catalase (Iwasaka et al, 2001). In studies from other laboratories, changes have been reported in the orientation of erythrocytes fixed with glutaraldehyde in field of 8 T (Higashi et al, 1996) and in the sedimentation rate of erythrocytes in a field of 6.3 T (Iino, 1997). Possible mechanisms for these and similar effects have been considered by ICNIRP (2004). Whether any of these phenomena may occur *in vivo* has yet to be determined (although see Taoka et al, 1997).

Biological uncertainties

45 It has been demonstrated that magnetic fields at millitesla levels and above can affect chemical reactions involving radical intermediates *in vitro* (McLauchlan, 1981; Grissom, 1995; Walleczek, 1995; Brocklehurst and McLauchlan, 1996; Brocklehurst, 1997). This raises the possibility that such effects might occur on metabolic reactions involving similar mechanisms, but this has not been demonstrated *in vivo* and the implications for human health are not clear (but see Watanbe et al, 1997, and Chigell and Sik, 1998; see also Adair, 1999, for a discussion of these mechanisms at environmental field levels). A similar argument applies to the various phenomena that have been reported *in vitro* with exposures at 8 T and above.

46 Much of the database consists of largely phenomenological observations, although the possibility of finding an effect seems to increase with field magnitude, particularly with exposures above 5–8 T. There is, however, insufficient evidence at present from animal and cellular studies to enable the thresholds for long-term effects from chronic exposure to static magnetic fields to be determined.

Summary

47 Cutaneous perception remains the most robust biological consequence of exposure to static electric fields. A threshold for perception was reported around 20 kV m^{-1} and annoying sensations were induced above about 25 kV m^{-1}. Painful spark discharges can be expected when a person who is well insulated from the ground touches a grounded object, or when a grounded person touches a conductive object that is well insulated from ground. However, the threshold static electric field values will vary depending on the degree of insulation and other factors. There is some suggestion that electrostatic fields associated with work with VDUs may aggravate existing skin conditions.

48 Very low frequency electric fields are induced in the body whenever movement of electrically conductive biological materials, such as blood, occurs in a static magnetic field. Vertigo, nausea, a metallic taste and phosphenes can be induced during movement of the head in static magnetic fields larger than about 2 T. In addition, flow potentials induced by the flow of blood in a magnetic field of this value have been calculated to generate electric fields of about 200 mV m^{-1} near the sino-atrial node of the heart during the relative refractory period of the cardiac cycle, when cardiac excitability is relatively low.

49 The effects of static magnetic fields have been investigated using a wide variety of animal models and exposure conditions. Apart from possible field dependent changes on localised blood flow in the skin, and on neuroendocrine effects associated with homing behaviour, no consistent effects have been reported using fields below 2 T, although the possibility of biological effects increases with exposure to fields of 5–8 T and above. There is little information regarding possible effects of chronic exposure.

50 There is little evidence suggesting that static magnetic fields of up to about 1 T are genotoxic, and while many *in vitro* data suggest that static magnetic fields are not carcinogenic, few *in vivo* studies have been carried out. Very few laboratory studies have investigated the effects of exposure to static electric fields. Overall, the available data remain insufficient to draw any firm conclusions regarding the carcinogenicity of static magnetic or electric fields.

The most plausible and coherent set of data from which guidance can be developed concerns perceptual and annoying responses in static electric fields and effects resulting from induced electric fields during movement in static magnetic fields. Other studies reviewed lack plausibility, coherence and consistency precluding a positive role in this process.

For static electric fields, any annoying and other stressful effects should be avoided if exposure is below the threshold for cutaneous perception of around 20 kV m^{-1}. Painful spark discharges can be expected when a person touches an object at a differing potential. However, the threshold field value under these circumstances will vary depending on the degree of insulation and other factors and will require specific assessment.

With regard to static magnetic fields, acute effects on the heart or nervous system associated with electric fields and flow potentials induced during movement in the field should not occur if exposures are less than 2 T. Particular caution should be applied with exposure to fields in excess of about 5–8 T.

There is insufficient evidence from animal and cellular studies to enable the thresholds for long-term effects from chronic exposure to static electric or magnetic fields to be determined.

4 Electromagnetic Fields of Frequencies Below 100 kHz

1 In this chapter, scientific data relevant to the development of exposure guidelines for time-varying electromagnetic fields (EMFs) of frequencies less than about 100 kHz are addressed. This range of frequencies is where the dominant and well-understood interaction processes and adverse health effects are due to electrostimulation of body tissues from induced internal electric fields and currents, although these processes occur up to about 10 MHz. However, the reviews summarised in this chapter cover a wide range of possible biological effects and disease outcomes. Thus this chapter summarises relevant published epidemiological, biological and computational dosimetry studies.

EPIDEMIOLOGY

2 The following subsections consider epidemiological studies of people exposed to extremely low frequency (30–300 Hz), including power frequency (50/60 Hz), electric and magnetic fields. These fields will be termed ELF EMFs in this document. Much of the associated research has examined the risk of cancer, and accordingly particular attention is given to this area. In addition, other health outcomes have been studied, including neurodegenerative diseases, suicide and depressive illness, cardiovascular disease, and reproductive outcome, and findings from these studies are also considered here. In doing so, references are made to published reviews of the relevant literature, together with citations to recent publications.

Cancer

3 The Advisory Group on Non-ionising Radiation (AGNIR) has periodically assessed epidemiological and experimental studies of exposures to ELF EMFs and the risk of cancer. A comprehensive assessment by AGNIR was recently published (AGNIR, 2001a). Other recent detailed reviews of this issue have also been performed by the International Agency for Research on Cancer (IARC, 2002) and by the Standing Committee on Epidemiology of the International Commission on Non-Ionizing Radiation Protection (Ahlbom et al, 2001).

4 Epidemiological studies reviewed previously by AGNIR (1992) suffered from a lack of measurement-based exposure assessments. Since then, considerable advances have been made in methods for assessing exposure. In particular, instrumentation allowing personal exposure to be measured has become widely available and has been used in many of the more recently published studies. This has provided a substantially improved basis for many of the epidemiological studies reviewed by AGNIR (2001a).

Residential exposures

5 Recent large and well-conducted studies have provided better evidence than was available in the past on the relationship between residential exposures to power frequency magnetic fields and the risk of cancer. A combined analysis, based on the

original data from nine key studies (Ahlbom et al, 2000), suggests that time-weighted average exposures of 0.4 μT or more are associated with a doubling of the risk of leukaemia in children under 15 years of age. However, the evidence is not conclusive. In studies in North America, the UK, Germany and New Zealand in which measurements were made, the extent to which the more heavily exposed children were representative is in doubt, owing to relatively low response rates for the controls (Ahlbom et al, 2000). Furthermore, in studies in the Nordic countries (Denmark, Finland, Norway and Sweden), for which the representativeness of the more heavily exposed children is assured, the fields were estimated and the results were based on such small numbers that the findings could have been due to chance. In the UK, very few children (perhaps 4 in 1000) are exposed to time-weighted average fields of 0.4 μT or more and a study in the UK (UK Childhood Cancer Study Investigators, 1999), with much the largest number of direct measurements of exposure, found no evidence of risk at lower levels. Nevertheless, the possibility remains that high and prolonged time-weighted average exposure to power frequency magnetic fields can increase the risk of leukaemia in children (AGNIR, 2001a). A recent study in Canada (Infante-Rivard and Deadman, 2003) reported a relative risk of childhood leukaemia following maternal occupational exposure during pregnancy to magnetic fields that was similar to that from the above combined analysis.

6 A study in the UK did not show an association between childhood cancer and measurements of electric fields in homes, although the precision of the findings based on fully validated measurements was generally low (Skinner et al, 2002).

7 Data on brain tumours come from some of the studies also investigating leukaemia and from others concerned exclusively with these tumours. AGNIR concluded that these data provided no comparable evidence of an association (AGNIR, 2001a). The ICNIRP Standing Committee on Epidemiology concurred in this view, and also concluded that there was no convincing evidence from studies in various countries of a relationship between childhood lymphoma and residential exposure to EMFs from nearby power lines (Ahlbom et al, 2001). There have been many fewer studies in adults. AGNIR found no reason to believe that residential exposure to EMFs was involved in the development of leukaemia or brain tumours in adults (AGNIR, 2001a). A recent analysis (Li et al, 2003) reported an association between elevated residential exposure to power frequency magnetic fields in Taiwan and an increase in the average age at diagnosis for adult patients with brain tumours, but not for leukaemia or breast cancer patients; this may represent a chance finding (Li et al, 2003). Also, studies of breast cancer and residential EMF exposures, based on measurements in the home, have generally not shown associations (Erren, 2001; Davis et al, 2002; Schoenfeld et al, 2003). Tynes et al (2003) reported an association between cutaneous malignant melanoma and estimated residential magnetic field exposures, but information was lacking on individual exposures to ultraviolet radiation, which is a known risk factor.

Occupational exposures

8 Studies of populations exposed occupationally to EMFs can include groups exposed generally at much higher levels than members of the public (AGNIR, 2001a). They may therefore have a greater potential to detect any adverse health effects, although they can be affected adversely by misclassification of exposures (Kheifets, 1999). Recently published studies of occupational exposure to EMFs and the risk of cancer are, in the

main, methodologically sound, and some of them are based on very large cohorts. AGNIR concluded that causal relationships between such exposures and an increase in tumour incidence at any anatomical site were not established (AGNIR, 2001a). The excesses, where they exist, are generally modest and are largely restricted to the two cancers noted in the 1992 AGNIR report, namely, leukaemia and brain cancer (AGNIR, 1992). Conflicting evidence exists for the particular cell types of leukaemia associated with the greatest risk but acute myeloid leukaemia is the most cited. The evidence of any risk for brain cancer is conflicting, even that from the most powerful of the studies (AGNIR, 2001a). More recent studies of workers exposed to EMFs have generally not shown raised risks of leukaemia or brain cancers (Harrington et al, 2001; Sorahan et al, 2001; Oppenheimer and Preston-Martin, 2002; Willett et al, 2003). A recent association reported in Canada (Villeneuve et al, 2002) between occupational magnetic field exposure and one particular type of brain tumour, namely glioblastoma multiforme, is not in accord with findings from another study conducted in Canada and France (Thériault et al, 1994).

9 Like AGNIR (2001a), the ICNIRP Standing Committee on Epidemiology concluded that the evidence linking occupational EMF exposure to adult leukaemia or brain tumours was weak (Ahlbom et al, 2001). In contrast, the California Department of Health Services Panel (Neutra et al, 2002) placed more weight on the epidemiological findings concerning adult brain cancers and EMFs. The ICNIRP Standing Committee on Epidemiology concluded that the evidence for links with occupational EMF exposure was also weak for breast cancer in men or women (Ahlbom et al, 2001). Furthermore, Erren (2001) has drawn attention to difficulties of probable misclassification of exposure and of possible misclassification of disease in interpreting studies of breast cancer. These points are relevant in view of suggested effects of EMF exposure on melatonin levels, as discussed further in paragraphs 50–52. Findings for some other cancer sites, such as the prostate (eg Thériault et al, 1994; Charles et al, 2003) and kidney (Håkansson et al, 2002), have been variable. In addition, the ICNIRP Standing Committee on Epidemiology considered the results from studies of childhood cancer and parental occupational exposure to EMFs to be inconsistent and unconvincing (Ahlbom et al, 2001).

10 The findings for breast and prostate cancer discussed above are relevant in view of suggested effects of EMF exposure on melatonin levels, as discussed in paragraphs 50–52. Reviews of studies of shift workers (Swerdlow, 2003) and of other studies of groups exposed to differing levels of light (Erren, 2002) have provided some suggestion that risks of certain types of cancer (eg breast and prostate) may be increased among those with suppressed melatonin levels due to light exposure. However, the interpretation of these results is not straightforward, owing to the possibility of confounding. For example, shift workers or blind persons may differ from reference populations not only in their exposures to light but also with respect to other determinants of health (Erren, 2002). AGNIR is currently examining the issue of melatonin, and the implications for assessments of EMFs and health.

Neurodegenerative diseases

11 AGNIR has reviewed epidemiological studies of ELF EMFs and the risk of neurodegenerative diseases (AGNIR, 2001b). These studies were mostly of people with occupational exposures. AGNIR concluded that there is no good ground for thinking that exposure to ELF EMFs can cause Parkinson's disease and only very weak evidence

to suggest that it could cause Alzheimer's disease. The evidence that people employed in electrical occupations have an increased risk of developing amyotrophic lateral sclerosis (ALS) is substantially stronger, but this could be because they run an increased risk of having an electric shock rather than any effect of long-term exposure to the fields *per se*. Similar conclusions were reached by the ICNIRP Standing Committee on Epidemiology (Ahlbom et al, 2001). The California Department of Health Services Panel (Neutra et al, 2002) tended to favour an association between ALS and ELF EMFs, whereas Li and Sung (2003) concluded that causal inferences were restricted because of the lack of direct information on EMF exposures and the incomplete consideration of other potential risk factors in the workplace. Two recent studies of mortality in occupational cohorts in Sweden have yielded somewhat conflicting results. Håkansson et al (2003a) reported raised risks of both ALS and Alzheimer's disease in relation to ELF magnetic fields, whereas in a larger cohort Feychting et al (2003) reported a raised risk for Alzheimer's disease but no increased risk (or even a decreased risk) of ALS in relation to magnetic fields. It is notable that the results of Håkansson et al (2003a) based on primary cause of death showed weaker evidence for an association in the case of Alzheimer's disease, whereas the findings for ALS were essentially unchanged. Thus, the quality of the information on diagnoses may have affected some of these findings, making their interpretation difficult.

Suicide and depressive illness

12 Risks of suicide and depressive illnesses have been examined in several studies of people exposed to power frequency EMFs occupationally or residentially. In a meta-analysis of such studies, Ahlbom (2001) concluded that the support for an association was weak. In its assessment of this topic, the ICNIRP Standing Committee on Epidemiology (Ahlbom et al, 2001) drew attention to a subsequent large occupational study that suggested an association with suicide (van Wijngaarden et al, 2000). A more recent occupational study, based on job titles recorded on death certificates, also suggested a weak association with suicide (van Wijngaarden, 2003). However, the exposure assessment here was not as detailed as that in the occupational studies of Baris et al, (1996), Johansen and Olsen (1998), and van Wijngaarden et al (2000), whose findings were variable. Overall, the ICNIRP Committee found it difficult to interpret the literature on suicide and depressive illnesses in relation to EMFs, owing in part to inconsistency in the findings (Ahlbom et al, 2001).

Cardiovascular disease

13 Several studies have examined cardiovascular disease and mortality among workers exposed to EMFs. In its review of these studies, the ICNIRP Standing Committee on Epidemiology concluded that evidence of cardiovascular effects due to elevated exposure to magnetic fields was weak (Ahlbom et al, 2001). This Committee also considered that an hypothesised association between such exposures and altered autonomic control of the heart – suggested by some human laboratory studies – remains speculative until corroborating evidence from further large epidemiological studies becomes available (Ahlbom et al, 2001). Two more recent occupational studies have not shown links between exposure to magnetic fields and either mortality from acute myocardial infarction (Sahl et al, 2002) or the incidence of severe cardiac arrhythmia (Johansen et al, 2002), whereas Håkansson et al (2003b) reported an association for mortality from acute myocardial infarction.

Other diseases

14 In 1994, AGNIR published a review of health effects related to the use of visual display units (VDUs) (AGNIR, 1994). It found that skin diseases did not appear to be caused by the EMFs from VDUs, although there was anecdotal evidence unsupported by epidemiology that in conditions of low humidity the associated static electric fields may aggravate existing skin problems and the strain of the actual work may give rise to skin problems among those with a predisposition to them. AGNIR found no evidence that work with VDUs resulted in a predisposition to the formation of cataracts, although there was an absence of long-term follow-up studies of users of VDUs. Minor opacities of the eye lens that do not affect visual acuity are to be expected among a large fraction of the population whether or not they use VDUs. Similar overall conclusions were reached by the International Non-Ionizing Radiation Committee (INIRC, now ICNIRP) of the International Radiation Protection Association in collaboration with the International Labour Organization (INIRC, 1994).

Reproductive outcome

15 In its 1994 report on health effects related to the use of VDUs, AGNIR reviewed nine epidemiological studies of spontaneous abortion and VDU use. Of these nine studies, six found no increase in risk, even in heavy users of VDUs, and three reported some increase in certain subgroups. The studies that showed no evidence of an increased risk of spontaneous abortion in VDU users had far fewer problems in their design and conduct than the ones reporting some increase in risk. Overall the results indicated that VDU use did not increase the risk of spontaneous abortion. AGNIR also concluded that the risk of congenital malformations did not appear to be increased in women who have used VDUs in early pregnancy. However, little information was available on the association of other adverse outcomes such as low birthweight with maternal VDU exposure. Some investigators had studied related exposures, such as domestic exposure to EMFs, and outcome of pregnancy. There was some suggestive evidence that work with, or the manufacture of, electrical appliances might be associated with an increased risk of prematurity, but this could be due to chemical exposures rather than exposure to EMFs. AGNIR concluded that the totality of the epidemiological and experimental evidence provided no good reason to suppose that low frequency EMFs encountered through the use of VDUs caused any harm to the fetus *in utero* (AGNIR, 1994). Similar conclusions were reached at around the same time by INIRC (1994). In a later review that also took account of more recent studies, the ICNIRP Standing Committee on Epidemiology found that the existing evidence did not support an association between maternal exposure to EMFs in the workplace and adverse pregnancy outcomes (Ahlbom et al, 2001).

16 Several studies have examined reproductive outcomes in relation to maternal residential exposures. Some of these studies have focused specifically on electrically heated beds. Concern has been expressed by, for example, the ICNIRP Standing Committee on Epidemiology about the potential for bias in retrospective studies that have been conducted (Ahlbom et al, 2001). These concerns relate both to the accuracy of assessing reproductive outcomes and to the quality of the information available on exposure. A more recent study by Lee et al (2002) that was largely conducted retrospectively had low response rates; associations that were reported with some

metrics measured at 30 weeks gestation are likely to be due to bias and/or chance, given the weak correlations with exposures early in pregnancy and the absence of an association with time-weighted average exposure (AGNIR, 2002). Only a few prospective studies have been conducted. One such study found no increasing trend in the risk of spontaneous abortion with intensity of use of electric bed heaters (Lee et al, 2000); another study gave inconsistent results for spontaneous abortion (Belanger et al, 1998) but no evidence of effects on birth weight or intrauterine growth retardation (Bracken et al, 1995) from the use of electrically heated beds. The ICNIRP Standing Committee on Epidemiology concluded that these studies do not support an association between maternal exposure to EMFs from heated beds and adverse pregnancy outcomes (Ahlbom et al, 2001). A subsequent prospective study (Li et al, 2002), which, together with the study of Lee et al (2002) was given strong weight by the California Department of Health Panel (Neutra et al, 2002) in its review, reported an association between spontaneous abortion and personal measurements of magnetic fields. However, the parameter that provided evidence of a risk – namely maximum magnetic field strength – was not chosen *a priori* on the basis of biological or epidemiological reasons to believe it might plausibly be of aetiological relevance (Li and Neutra, 2002); the results were sensitive to the choice of breakpoint, which was made on the basis of the observed data; and the study was not a standard prospective study as more than half the spontaneous abortions (and all those at all strongly related to maximum field exposure) occurred before the measurements were made, the compliance rate was low, and the possibility of selection bias was not excluded (AGNIR, 2002).

17 There has been little epidemiological research on male fertility in relation to exposure to power frequency EMFs. The few occupational studies conducted have examined job titles, but have lacked individual measurements of field levels. Results from these studies have been variable (eg Lundsberg et al, 1995; Irgens et al, 1999) and do not provide convincing evidence of an association. Studies of birth defects in relation to parental occupational exposures and to maternal residential exposures (eg Blaasaas et al, 2002, 2003) have also been limited by a lack of magnetic field measurements, as well as by the potential for chance findings due to studying many outcomes.

Epidemiological uncertainties

18 Many of the epidemiological studies of groups exposed to ELF EMFs have been case–control studies. Their retrospective nature has led to concerns in some instances about the possibility of associated sources of bias. For example, some of the case–control studies of childhood leukaemia and residential exposures that were included in the combined analysis of Ahlbom et al (2000) may have been affected by the relatively low response rates for controls. This potential problem did not affect all of the studies in the combined analysis – in particular, studies in the Nordic countries, which were based on national population registers. However, the statistical precision of findings from the Nordic studies was limited at higher exposure levels.

19 Follow-up studies of workers based on well-defined cohorts and with objective measures of exposure and health should also be less susceptible to retrospective sources of bias. However, there can be difficulties in these studies in estimating exposures many years after the event. Furthermore, other types of exposure may arise in the workplace which are correlated with EMF exposure and which may affect the

health of workers. An example concerns exposure to welding fumes, which may increase lung cancer risks among welders (Stern, 1987).

20 Meta-analyses of findings from different studies or more detailed combined analyses based on the original data from these studies have helped in increasing statistical precision and in examining the compatibility of findings – for example, in highlighting the inconsistency of results on childhood leukaemia and residential magnetic field exposure (Ahlbom et al, 2000). However, such analyses have also highlighted inconsistencies in results between studies, so emphasising the need for caution when drawing conclusions: for example, concerning depressive illnesses and EMFs (Ahlbom, 2001).

21 Some studies of reproductive outcome and EMF exposure are likely to have been affected by biases associated with their retrospective nature, namely, differential recall of exposure and reproductive history. Consequently, prospective studies that have been performed of such outcomes – whilst rarer than retrospective studies – should generally be more reliable. It should also be noted that several exposure measures and various outcomes have been considered in some studies. In the absence of a strong *a priori* basis for these multiple hypotheses, it is difficult to interpret any positive findings.

Summary

22 There is some epidemiological evidence that time-weighted average exposure to power frequency magnetic fields above 0.4 μT is associated with a small increase in the absolute risk of leukaemia in children, from about 1 in 20 000 to 1 in 10 000 per year. On a relative scale, this corresponds to a doubling of the risk. Such exposures are seldom encountered by the general public in the UK, and the raised risk – if it were real – would correspond roughly to an additional two cases of childhood leukaemia per year in the UK, compared with an annual total of around 500 cases. In the absence of clear evidence of a carcinogenic effect in adults, or of a plausible explanation from experiments on animals or isolated cells, AGNIR has concluded that the epidemiological evidence is currently not strong enough to justify a firm conclusion that such fields cause leukaemia in children. However, the possibility remains that intense and prolonged exposures to magnetic fields can increase the risk of leukaemia in children, unless further research indicates that the finding is due to chance or some currently unrecognised artefact (AGNIR, 2001a). The ICNIRP Standing Committee on Epidemiology reached a similar conclusion, and took the view that, among all the outcomes evaluated in epidemiological research of EMFs, childhood leukaemia in relation to postnatal exposures to fields above 0.4 μT is the one for which there is most evidence of an association. This result is unlikely to be due to chance but may be, in part, due to bias, and is difficult to interpret in the absence of a known mechanism or reproducible experimental support (Ahlbom et al, 2001). The International Agency for Research on Cancer (IARC, 2002) judged that this finding provided limited evidence for an excess risk in humans exposed at these levels, and it evaluated ELF magnetic fields as being 'possibly carcinogenic to humans' (Classification 2B). IARC also concluded that for the vast majority of children, who were exposed to residential magnetic fields less than 0.4 μT, there was little evidence of any increased risk of leukaemia. Furthermore, IARC considered the evidence for excess cancer risks of all other kinds, in children and adults, as a result of exposure to ELF electric and magnetic fields to be inadequate.

23 Studies of occupational exposure to ELF EMFs do not provide strong evidence of associations with neurodegenerative diseases. The only possible exception concerns people employed in electrical occupations who appear to have an increased risk of developing amyotrophic lateral sclerosis; however, this may be due to effects of electric shocks rather than any effect of long-term exposure to the fields *per se*. Studies of suicide and depressive illness have given inconsistent results in relation to ELF EMF exposure, and evidence for a link with cardiovascular disease is weak. Skin diseases do not appear to be caused by EMFs from visual display units (VDUs), although existing skin conditions may be aggravated, and work with VDUs does not appear to cause a predisposition to the formation of cataracts. The overall evidence from studies of maternal exposure to ELF EMFs in the workplace does not indicate an association with adverse pregnancy outcomes, while studies of maternal exposure in the home are difficult to interpret. Results from studies of male fertility and of birth outcome and childhood cancer in relation to parental occupational exposure to ELF EMFs have been inconsistent and unconvincing.

The epidemiological evidence indicates that exposure to power frequency magnetic fields above 0.4 μT is associated with a small absolute raised risk of leukaemia in children (an approximate doubling of the relative risk). However, the evidence is not strong enough to justify a firm conclusion that such fields cause leukaemia in children.

There is little evidence to suggest that the risk of childhood leukaemia might be increased by exposure to ELF magnetic fields of time-weighted average magnetic flux density below 0.4 μT, or that raised cancer risks of other types, in children and adults, might arise as a result of exposure to ELF magnetic fields. Information specifically on electric fields is more sparse.

The findings from studies of health outcomes other than cancer have generally been inconsistent or difficult to interpret.

Workers in electrical occupations do appear to have an increased risk of developing amyotrophic lateral sclerosis, but this may be due to effects of electric shocks rather than any effect of long-term exposure to ELF EMFs *per se*.

Whilst skin diseases do not appear to be caused by EMFs from VDUs, existing skin conditions may be aggravated by the associated static electric fields.

The results of epidemiological studies, taken individually or as collectively reviewed by expert groups, cannot be used as a basis for the derivation of quantitative restrictions on exposure to EMFs.

BIOLOGY

24 The biological effects of low frequency EMFs continue to be studied using a wide variety of exposure conditions, models and biological endpoints. While this research has produced some useful information in helping to formulate public health policy, a number of uncertainties and possibilities remain to be resolved, especially regarding the consequences of exposure at levels commonly encountered in the environment. Many of the same controversies that existed a decade ago continue to this day. The absence of any established mechanism to describe interactions of very weak fields with living tissue still presents a major hurdle to formulating hypotheses suitable for testing.

25 This section presents a summary of the biological effects of time-varying EMFs with frequencies less than 100 kHz. It takes account of the consensus of the many national and international scientific expert groups that have comprehensively reviewed the biological effects literature. These include AGNIR (1994, 2001a), IARC (2002), ICNIRP (1997, 1999a, 2004), NIEHS (1998, 1999) and NRC (1997).

26 It is clear from these reviews that the effects of surface electric charge and of induced electric fields and currents represent the most suitable biological bases for formulating restrictions on human exposure to EMFs. These effects, and the different susceptibilities of people of varying health status, are summarised here.

27 In addition to these well-understood effects, a large number of other biological effects have sometimes been reported. Most of these can be grouped together into effects on cancer and carcinogenic processes, effects on the developing embryo and fetus, and neurobehavioural effects (although these broad categories are neither exhaustive nor mutually exclusive). The possibility of field dependent effects in these areas has also been reviewed by the various scientific expert groups. None of these effects was considered sufficient to form a suitable basis for deriving quantitative restrictions on exposure. These studies are summarised here.

Effects of surface charge and induced electric fields and currents

28 An electric charge is induced on the surface of a person (or other living organism) exposed to a low frequency electric field and this charge alternates in amplitude with the frequency of the applied field. The effects of the surface electric charge *per se* are well understood and have been used in the formulation of guidance on restrictions on low frequency electric field exposure. The alternation of the surface charge with time induces an electric field and therefore current flow within the body; in addition, exposure to a low frequency magnetic field induces internal electric fields and circulating currents. If of sufficient magnitude, these induced electric fields and currents can affect electrically excitable nerve and muscle tissue.

29 Guidance on restrictions on exposure to low frequency electric and magnetic fields has been formulated from a consideration of the basic physiological properties of electrically excitable tissue, particularly the central nervous system (CNS), and of physiological responses to relatively intense low frequency magnetic fields. The evidence for these acute effects is summarised here; a more detailed account of the electrophysiological evidence was prepared by an ad hoc expert group on weak electric fields convened at NRPB in November 2001 (Appendix A) and was presented at an ICNIRP/WHO workshop in March 2003 (ICNIRP/WHO, 2003; Appendix B).

Surface electric charge responses

30 Surface electric charge can be perceived directly through the induced vibration of body hair and tingling sensations in areas of the body, particularly the arms, in contact with clothing, and indirectly through spark discharges between a person and a conducting object within the field. In several studies carried out in the 1970s and 1980s (summarised by Reilly, 1998, 1999), the threshold for direct perception has shown wide individual variation; 10% of exposed subjects had detection thresholds of around 2–5 kV m^{-1} at 60 Hz, whereas 50% could detect fields of 7–20 kV m^{-1}. These effects were considered annoying by 5% of the test subjects exposed under laboratory conditions above electric field strengths of about 15–20 kV m^{-1}.

31 In addition to showing a wide variation in individual sensitivity, these responses also vary with environmental conditions, particularly humidity. The studies referred to above, however, included both wet and dry exposure conditions.

32 It has been estimated that spark discharges would be painful to 7% of subjects who are well insulated from ground and who touch a grounded object within a 5 kV m^{-1} field (Reilly, 1998, 1999), whereas they would be painful to about 50% in a 10 kV m^{-1} field. Unpleasant spark discharges can also occur when a grounded person touches a large conductive object such as a large vehicle that is well-insulated from ground and is situated within a strong electric field. Here, the threshold field strength required to induce such an effect varies inversely with the size of the conductive object. In both cases, the presence in the 'well-insulated' person or object of a conductive pathway to ground would tend to mitigate the intensity of any effect (Reilly, 1998, 1999), as would the impedance to earth of the 'grounded' object or person.

Exposure to power frequency electric fields causes well-defined biological responses through surface electric charge effects. These responses depend on field strength, ambient conditions as well as individual sensitivity, and range from perception to annoyance.

Thresholds for direct perception by 10% of volunteers ranged between 2 and 5 kV m^{-1}; 5% found 15–20 kV m^{-1} annoying.

For spark discharges, the discharge from a person to ground is painful to 7% of volunteers in a field of 5 kV m^{-1}.

Thresholds for the discharge from an object through a grounded person depend also on the size of the object and therefore require specific assessment.

Acute electrophysiological responses

33 Studies have been carried out of direct nerve stimulation thresholds in volunteers by intense, pulsed magnetic fields. The effects of exposure inducing weak electric fields, below the threshold for direct nerve stimulation, can be assessed from electrophysiological studies of weak electric field interactions with nerve tissue and studies of retinal and cognitive function in volunteers.

34 These various effects result from the interaction of the induced electric field with voltage-gated ion channels. These are ion channels in cell membranes that allow the passage of particular ionic species across the cell membrane in response to the opening of a 'gate' which is steeply sensitive to the transmembrane voltage (eg Catterall, 1995; Hille, 2001; Mathie et al, 2003). Sensitivity is therefore primarily to the transmembrane electric field and varies widely between different ion channels (Hille, 2001; Saunders and Jefferys, 2002; Mathie et al, 2003). Many voltage-gated ion channels are associated with electrical excitability and electrical signalling. Such electrically excitable cells not only comprise neurons, glial and muscle cells, but also endocrine cells of the anterior pituitary, adrenal medulla and pancreas, gametes and, with reservations, endothelial cells (Hille, 2001). All these cells generally express voltage-gated sodium and calcium channels. Both of these ion channels are involved in electrical signalling and calcium ions activate a number of crucial cellular processes including neurotransmitter release, excitation-contraction coupling in muscle cells and gene expression (Catterall, 2000; Hille, 2001). Some ion channels exist in other, non-excitable tissues such as those in the

kidney and liver which show slow electric potential changes but their voltage sensitivity is likely to be lower (eg Jan and Jan, 1989; Begenisich and Melvin, 1998; Catterall, 2000; Cahalan et al, 2001; Nilius and Droogmans, 2001). Since voltage-gated ion channels are steeply sensitive to the transmembrane electric potential, electric field strength in tissue is a more relevant parameter to relate to electrically excitable cell thresholds than current density (Blakemore et al, 2003). A similar view regarding the merits of electric field strength as the more relevant dosimetric quantity had been expressed previously at a workshop on exposure guidelines for low frequency electric and magnetic fields (Sheppard et al, 2002), and is incorporated into the IEEE C95.6 standard limiting human exposure to ELF EMFs (IEEE, 2002).

Stimulation effects in high fields

35 Large, rapidly changing, pulsed magnetic fields used in various specialised medical applications such as MRI and transcranial magnetic stimulation (TMS) can induce electric fields able to stimulate nervous tissue in humans. Minimum, orientation-dependent stimulus thresholds for large diameter (20 μm) myelinated nerve axons have been estimated (Reilly, 1998, 1999) to lie around 6 V m^{-1} at frequencies up to about 1–3 kHz. In addition, accommodation to a slowly changing stimulus resulting from slow inactivation of sodium channels will raise thresholds at low frequencies. In MRI, nerve stimulation is an unwanted side-effect of a procedure used to derive cross-sectional images of the body for clinical diagnosis (see Shellock, 2001). In TMS, parts of the brain are deliberately stimulated in order to produce a transient, functional impairment for use in the study of cognitive processes (see Reilly, 1998; Walsh and Cowey, 1998; Ueno, 1999). Threshold rates of change of MRI switched gradient magnetic fields for perception, discomfort and pain resulting from peripheral nerve stimulation are extensively reviewed by Nyenhuis et al (2001). Median minimum threshold rates of change of magnetic field (during periods of less than 1 ms) for perception were generally 15–25 T s^{-1} depending on orientation and showed considerable variation between individuals (Bourland et al, 1999). These values were somewhat lower than those previously estimated by Reilly (1998, 1999), possibly due to the constriction of eddy current flow by high impedance tissue such as bone (Nyenhuis et al, 2001). Thresholds rose as the pulse width of the current induced by the switched gradient field decreased; the median pulse width (the chronaxie) corresponding to a doubling of the minimum threshold (the rheobase) ranged between 360 and 380 μs (Bourland et al, 1999).

36 In TMS, brief, localised, suprathreshold stimuli are given, typically by discharging a capacitor through a coil situated over the surface of the head, in order to stimulate neurons in a small volume (a few cubic centimetres) of underlying cortical tissue (Reilly, 1998). The induced current causes the neurons within that volume to depolarise synchronously, followed by a period of inhibition (Fitzpatrick and Rothman, 2000). When the pulsed field is applied to a part of the brain thought to be necessary for the performance of a cognitive task, the resulting depolarisation interferes with the ability to perform the task. In principle then, TMS provides cognitive neuroscientists with the capability to induce highly specific, temporally and spatially precise interruptions in cognitive processing – sometimes known as 'virtual lesions'. Reilly (1998) noted induced electric field thresholds to be around 20 V m^{-1}. However, Walsh and Cowey (1998) cited typical rates of change of magnetic field of 30 kT s^{-1} over a 100 μs period transiently inducing an electric field of 500 V m^{-1} in brain tissue.

37 People are likely to show variations in sensitivity to induced electric fields. In particular, epileptic syndromes are characterised by increased neuronal excitability and synchronicity (Engelborghs et al, 2000); seizures arise from an excessively synchronous and sustained discharge of a group of neurons (Jefferys, 1994; Engelborghs et al, 2000). TMS is widely used, apparently without adverse effects. However, repetitive TMS has been observed to trigger epileptic seizure in some susceptible subjects (Wassermann 1998; Fitzpatrick and Rothman, 2000). These authors also reported short- to medium-term memory impairments and noted the possibility of long-term cognitive effects from altered synaptic activity or neurotransmitter balance. Contraindications for TMS use agreed at an international workshop on repetitive TMS safety (Wassermann, 1998) include epilepsy, a family history of seizure, the use of tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold. Serious heart disease and increased intracranial pressure have also been suggested as contraindications due to the potential complications that would be introduced by seizure.

Electric field strength in tissue is a more relevant parameter to relate to electrically excitable cell thresholds than current density. Threshold induced electric field strengths for direct nerve stimulation lie, in theory, in the range 5–25 V m^{-1}; apparent thresholds can be somewhat lower due to the preferential flow of current through tissues with relatively high electrical conductivity. These thresholds are likely to be constant between a few hertz and a few kilohertz.

An increased sensitivity of brain nerve tissue to induced electric fields seems likely to be associated with epilepsy, a family history of seizure, the use of tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold. Serious heart disease and increased intracranial pressure have also been suggested as contraindications due to the potential complications that would be induced by seizure.

Electrophysiological studies of weak field effects

38 Cells of the central nervous system are considered to be sensitive to induced ELF electric fields at levels that are below the threshold for impulse initiation in nerve axons (Jefferys, 1995; Saunders and Jefferys, 2002; Jefferys et al, 2003; Saunders, 2003). Such weak electric field interactions have been shown in experimental studies mostly using isolated animal brain tissue, to result from the extracellular voltage gradients generated by the synchronous activity of a number of neurons, or from those generated by applying pulsed or alternating currents directly through electrodes placed on either side of the tissue. Jefferys and colleagues (Jefferys, 1995; Jefferys et al, 2003) identified *in vitro* thresholds of around 4–5 V m^{-1}. Essentially, the extracellular gradient alters the potential difference across the neuronal membrane with opposite polarities at either end of the neuron; a time constant of a few tens (15–60) of milliseconds results from the capacitance of the neuronal membrane (Jefferys et al, 2003) and indicates a limited frequency response. Similar arguments concerning the limited frequency response of weak electric field effects due to the long time constants (25 ms) arising from cell membrane capacitance have been given by Reilly (2002) regarding phosphene data and have been incorporated into the IEEE C95.6 standard limiting human exposure to EMFs up to 3 kHz (IEEE, 2002); see paragraph 46.

39 The CNS *in vivo* is likely to be more sensitive to induced low frequency electric fields and currents than *in vitro* preparations (Saunders and Jefferys, 2002). Spontaneous activity is higher, and interacting groups or networks of nerve cells exposed to weak electrical signals would be expected, on theoretical grounds, to show increased sensitivity through improved signal-to-noise ratios compared with the response of individual cells (Valberg et al, 1997; Sterling, 1998; Adair, 2001). Much of normal cognitive function of the brain depends on the collective activity of very large numbers of neurons. Neural networks are thought to have complex non-linear dynamics that can be very sensitive to small voltages applied diffusely across the elements of the network (Adair, 2001; Jefferys et al, 2003; ICNIRP, 2004). Jefferys and colleagues recently reported preliminary results from a study of the effects of 50 Hz electric fields on the electrical activity of hippocampal tissue in which a large number of interacting neurons were induced into coherent oscillatory behaviour by the application of a glutamate receptor stimulant (Saunders, 2003). The weakest applied sinusoidal field that could modulate the induced electrical oscillation was reported to be 2 V m^{-1} (peak-to-peak); further study is in progress. Gluckman et al (2001) placed the detection limit for network modulation in hippocampal slices by electric fields at around 100 mV m^{-1}. Recent experimental work by Francis et al (2003) confirmed a neural network threshold of around 140 mV m^{-1}, more sensitive than the average single neuron threshold of 185 mV m^{-1} in their study. A lower limit on neural network sensitivity to physiologically weak induced electric fields has been considered elsewhere on theoretical grounds to be around 1 mV m^{-1} (Adair et al, 1998a; Veyret, 2003). The time-course of the opening of the fastest voltage-gated ion channels can be less than 1 ms (Hille, 2001), suggesting that effects at frequencies up to a few kilohertz should not be ruled out. Accommodation to a slowly changing stimulus resulting from slow inactivation of the sodium channels will raise thresholds at frequencies less than around 10 Hz.

40 People suffering from or predisposed to epilepsy are likely to be more susceptible to induced low frequency electric fields in the CNS (Blakemore et al, 2003). Jefferys (1994) estimated that around 1000 neurons are the minimum aggregate for epileptic activity.

41 Other electrically excitable tissues with the potential to show network behaviour include glial cells located within the CNS (eg Parpura et al, 1994), and the autonomic and enteric nervous systems (see Sukkar et al, 2000), which comprise interconnected non-myelinated nerve cells and are distributed throughout the body and gut, respectively. These systems are involved in regulating the visceral or 'housekeeping' functions of the body; for example, the autonomic nervous system is involved in the maintenance of blood pressure. Muscle cells also show electrical excitability; only cardiac muscle tissue has electrically interconnected cells. However, Cooper et al (2003), in a review of cardiac ion channel activity, concluded that weak internal electric fields much below the excitation threshold were unlikely to have any significant effect on cardiac physiology. EMF effects on the heart (eg Sastre et al, 2000) could nevertheless result from indirect effects mediated via the autonomic nervous system and CNS (Sienkiewicz, 2003). Effects on the endocrine system could potentially also be mediated this way, although the evidence from volunteer experiments indicated that acute low frequency magnetic field exposure up to 20 μT did not influence the circadian variation

in circulating levels of melatonin (Warman et al, 2003), nor other plasma hormone levels (ICNIRP, 2004).

42 Electric fields around 10–100 V m^{-1} generated by physiological and metabolic processes within the body can affect nerve growth *in vitro* and *in vivo* and may play an important role in normal developmental processes (Nuccitelli, 1992, 2003). Electric fields of a similar order, generated by passing direct currents between electrodes placed on either side of the preparation, have been reported to affect development of the embryonic and neonatal nervous system and nerve regeneration (eg AGNIR, 1994; Jefferys, 1995; Nuccitelli, 2003). However, other authors (Borgens, 1999; Moriarty and Borgens, 2001) have reported that electric fields of only 100 mV m^{-1} can influence the regeneration of nerve fibres in the spinal cord and that application of an electric field of 320 mV m^{-1} that alternated in polarity every 15 minutes could affect the density and orientation of astrocytes in an injured mammalian spinal cord. Generally, however these processes are far less sensitive to the effects of low frequency fields (Sienkiewicz, 2003) and experimental studies do not reveal adverse EMF effects on mammalian development (Juutilainen, 2003).

Weak electric field interactions can be demonstrated in CNS tissue *in vitro* around 4–5 V m^{-1}; time constants are typically around tens of milliseconds. *In vivo*, greater susceptibility is predicted due to the larger number of interacting nerve cells or neural networks; the data available are consistent with a threshold of 100 mV m^{-1}. Thresholds may be constant between a few hertz and a few kilohertz. Electrically excitable tissues with the potential to show network behaviour include nerve and glial cells of the CNS and the autonomic and enteric nervous system. People suffering from or predisposed to epilepsy are likely to be more susceptible to induced low frequency electric fields in the CNS.

Other excitable tissues such as the heart seem less susceptible to the direct effects of weak induced low frequency electric fields, but may be affected indirectly via effects on the CNS. Applied static electric fields also affect nerve growth and regeneration. In addition, static electric fields of typically 10–100 V m^{-1} have been reported to affect the development of the embryonic and neonatal nervous system; however, these processes are likely to be less sensitive to the effects of induced low frequency electric fields. Nevertheless, effects have been seen with applied static electric fields as low as 100 mV m^{-1} and at higher values of applied static electric fields which alternate slowly. These data indicate that a degree of caution is appropriate when considering the potential susceptibility of the developing nervous system, both *in utero* and in neonates and young children to weak induced time-varying electric fields.

Volunteer studies of weak field effects

43 A number of volunteer studies have been carried out on the effects of magnetically induced or directly applied low frequency electric currents below levels for direct nerve stimulation on retinal* function; also on learning, memory and other cognitive functions. Some of these have involved conditions where the induced or applied currents were mostly around or above the average 'bulk' endogenous brain tissue

* The neural circuitry of the retina forms part of the central nervous system (Dowling, 1987).

current density levels of 1–10 mA m^{-2} (Bernhardt, 1988; Wachtel, 1992). The equivalent electric fields would be around 10–100 mV m^{-1}, assuming a conductivity of brain tissue of around 0.1 S m^{-1}. The experimental evidence is summarised immediately below. Most studies, however, have investigated possible effects resulting from very much lower levels of exposure; these are summarised in paragraphs 50–54 and 86–100.

44 The effects of exposure to weak low frequency magnetic fields on human retinal function are well established. Exposure of the head to magnetic flux densities above about 5 mT at 20 Hz, rising to about 15 mT at 50 Hz, will reliably induce faint flickering visual sensations called magnetic phosphenes (Sienkiewicz et al, 1991; Attwell, 2003; Taki et al, 2003). It is generally agreed that these phosphenes result from the interaction of the induced electric current with electrically sensitive cells in the retina. Several lines of evidence suggest the production of phosphenes by a weak induced electric field does not involve the initial transduction of light into an electrical signal. Firstly, the amplification of the initial signal generated by the absorption of light takes place primarily through an intracellular 'second-messenger cascade' of metabolic reactions prior to any change in ion channel conductivity (Hille, 2001). Secondly, the phosphene threshold appears unaffected by 'dark' adaptation to low light levels (Carpenter, 1972). In addition, phosphenes have been induced in a patient with retinitis pigmentosa, a degenerative illness primarily affecting the pigment epithelium and photoreceptors (Lövsund et al, 1980).

45 There is good reason to view retinal circuitry as a conservative model for induced electric field effects on CNS neuronal circuitry in general (Attwell, 2003). Firstly, the retina displays all the processes present in other CNS areas, such as graded voltage signalling and action potentials, and has a similar biochemistry. Secondly, in contrast to more subtle cognitive effects, phosphenes represent a direct and reproducible perception of field interaction. A clear distinction can be made in this context between the detection of a normal visual stimulus and the abnormal induction of a visual signal by non-visual means (Saunders, 2003); the latter suggests the possibility of direct effects on cognitive processes elsewhere in the CNS.

46 Thresholds for electrically induced phosphenes* have been estimated to be about 10–14 mA m^{-2} at 20 Hz (Adrian, 1977; Carstensen et al, 1985). A similar value (10 mA m^{-2} at 20 Hz), based on studies of magnetically induced phosphenes, has been derived by Wake et al (1998). The equivalent electric field threshold can be estimated as around 100–140 mV m^{-1} using a tissue conductivity for brain tissue of about 0.1 S m^{-1} (Gabriel, 1995). More recently, Reilly (2002) has calculated an approximate 20 Hz electric field threshold in the retina of 53 mV m^{-1} for phosphene production. A similar value (60 mV m^{-1}) has been reported elsewhere (see Saunders, 2003). Subsequently, however, Taki et al (2003) indicated that calculations of phosphene thresholds suggested that electrophosphene thresholds were around 100 mV m^{-1}, whereas magneto-phosphene thresholds were around 10 mV m^{-1} at 20 Hz. More detailed calculation by Attwell (2003) based on neuro-anatomical and physiological considerations, suggested that the phosphene electric field threshold in the extracellular fluid of the retina was in the range 10–60 mV m^{-1} at 20 Hz. There is however, considerable uncertainty attached

* Carstensen et al (1985) applied an incorrect brain tissue conductivity value (0.01 S m^{-1}); the correct value has been used above to calculate phosphene threshold current density.

to these values. In addition, the extrapolation of values in the extracellular fluid to those appropriate for whole tissue, as used in most dosimetric models, is complex, depending critically on the extracellular volume and other factors. With regard to the frequency response, Reilly (2002) suggested that the narrow frequency response was the result of relatively long membrane time constants of around 25 ms (see paragraph 38). However, at present, the exact mechanism underlying phosphene induction is unknown. It is not clear whether the narrow frequency response is due to intrinsic physiological properties of the retinal neurons, as suggested by Reilly (2002) above and by Attwell (2003) considering active amplification process in the retinal neuron synaptic terminals, or is the result of central processing of the visual signal (Saunders and Jefferys, 2002; Saunders, 2003). This issue can only be resolved through further investigation.

47 Two groups (Stollery et al, 1985, 1986, 1987; Preece et al, 1998) have studied the psychological effects of induced 50 Hz electric fields and currents comparable to those which at lower frequencies can induce phosphenes (5–15 mT) – studies of volunteers exposed to lower magnetic flux densities are described in paragraphs 50–54. Stollery et al (1985, 1986, 1987) exposed volunteers on two separate days to a 50 Hz electric field of 36 kV m^{-1}; the peak induced current density in the brain was calculated (Edwards and Pickles, 1985; Edwards, 1986) to be between 10 and 40 mA m^{-2} (100 and 400 mV m^{-1} using a conductivity of 0.1 S m^{-1}). Cognitive function and mood were assessed using questionnaires and a battery of computer-generated cognitive tests. No obvious or simple mental deficit resulted from the passage of the current but levels of arousal and the response time for some tests of linguistically complex (syntactic) reasoning were significantly affected in one group of subjects but not in another. Overall the results were inconclusive. More recently, Preece et al (1998) found significant effects on some aspects of cognitive function in volunteers during exposure to 50 Hz magnetic fields of 0.6 mT. Current densities induced in the head were estimated as about 2 mA m^{-2}, peaking at 6 mA m^{-2} (20 mV m^{-1} and 60 mV m^{-1} using a conductivity of 0.1 S m^{-1}). The authors reported that exposure to 50 Hz magnetic fields caused a decline in numeric working memory sensitivity and a decline in word recognition sensitivity. In addition, the volunteers were less accurate, although not slower, than controls on the choice reaction time task. Thus, Preece et al (1998) reported impairments in three important cognitive functions – attention, working memory and episodic secondary memory – during exposures inducing peak electric fields of between 20 and 60 mV m^{-1}; the dosimetric rigour with which these values were derived is not, however, clear.

The retina is considered to be a good model of the sensitivity of CNS tissue to induced electric fields. Retinal function can be reliably affected by exposure to ELF magnetic fields and applied electric currents; threshold electric field strengths in the extracellular fluid of the retina have been estimated to lie between about 10 and 60 mV m^{-1} at 20 Hz. There is considerable uncertainty attached to these values. In addition, their extrapolation to those appropriate for the whole tissue, as used by dosimetric models, is complex and uncertain. The mechanisms underlying the variation of the threshold of this perceptual response with frequency are unknown.

Other possible effects

48 In addition to the surface charge effects and electrophysiological responses described above, the possibility that exposure to low frequency EMFs may induce other biological effects has continued to be investigated. Many different models, including volunteers, animals and cultures of cells have been examined using a wide range of tests and exposure conditions (NIEHS, 1999). However, it is conceptually useful to group all these studies into three broad categories (Sienkiewicz et al, 1993; NRC, 1997) and to consider effects on cancer, reproduction and development, and neurobehavioural effects. The experimental evidence for these possibilities is summarised here. Very detailed reviews, critiques and summaries of this literature have been published elsewhere by national and international expert groups (AGNIR, 1994, 2001a; IARC, 2002; ICNIRP, 1997, 1999a, 2004; NIEHS, 1998, 1999; NRC, 1997).

Cancer

49 The majority of the experimental studies conducted over the last ten years investigating the biological effects of EMFs have focused on the carcinogenic potential of power frequency magnetic fields. Few studies have used electric fields. Most of this research has been conducted at the cellular and animal level, and studies with volunteers have tended to concentrate on the effects of exposure on melatonin.

Volunteer studies

50 It has been suggested that chronic exposure to EMFs may disrupt pineal physiology and decrease circulating levels of melatonin and thereby increase the risk of breast cancers and other tumours (Stevens, 1987, 1994). Several mechanisms for this have been postulated, including modulation of immune responsiveness and decreased scavenging of free-radicals (see Cridland et al, 1996a). AGNIR is currently undertaking a review of the effects of EMFs on melatonin and breast cancer.

51 The evidence suggests that human melatonin rhythms are not significantly delayed or suppressed by exposure to magnetic fields (NIEHS, 1998; AGNIR, 2001a; IARC, 2002; although also see Karasek and Lerchl, 2002). Wilson et al (1990) reported that chronic exposure to the pulsed fields generated by mains or DC powered electric blankets had no effect on urinary excretion of the major metabolite of melatonin, 6-hydroxy-melatonin sulphate. Transient increases in night-time excretion were reported in 7 out of 28 volunteers in the periods following the onset and cessation of use of one type of blanket, although the particular relevance of this result is questionable (AGNIR, 2001a). Similarly, night-time exposure to continuous or intermittent power frequency magnetic fields for 1 or 2 nights had no effect on melatonin metabolism as measured by salivary melatonin levels (Griefahn et al, 2002), serum melatonin levels or the excretion of 6-hydroxymelatonin sulphate (Graham et al, 1996, 1997, 2001a,b; Selmaoui et al, 1997; Åkerstedt et al, 1999; Crasson et al, 2001; Kurokawa et al, 2003). However, the results of a study investigating the effects of night-time exposure to 60 Hz fields for 4 nights (Graham et al, 2000a) suggested a weak cumulative effect of exposure. Exposed subjects showed more intra-individual variability in the overnight levels of excretion of melatonin or 6-hydroxymelatonin sulphate on night 4, although there was no overall effect on levels of melatonin. Hong et al (2001) also reported no significant field dependent effects on melatonin rhythms in men following 11 weeks of night-time exposure.

52 Wood et al (1998) suggested that exposure to circularly polarised power frequency magnetic fields prior to the night-time rise in melatonin may delay the onset of the rise by about half an hour, and reduce peak levels possibly in a sensitive subgroup of the study population. This preliminary study is suggestive of an effect, although it has been criticised for procedural and other difficulties (AGNIR, 2001a).

53 In addition to laboratory studies, several studies have looked at endocrine function in humans exposed to power frequency magnetic fields in occupational and residential settings (Pfluger and Minder, 1996; Burch et al, 1998, 1999, 2000; Juutilainen et al, 2000; Davis et al, 2001). In a review, IARC (2002) noted that these studies reported some perturbation in the excretion of 6-hydroxymelatonin sulphate in exposed groups. However, these small reductions were not consistent across studies and the exposure parameters differed between studies. IARC (2002) concluded that it was difficult to distinguish between effects of magnetic fields and those of other environmental factors. The particular difficulties associated with investigating effects of EMFs on melatonin are discussed by Warman et al (2003).

54 Finally, a few laboratory studies have investigated effects of magnetic fields on other endocrine and haematological function and immune system. No field dependent effects have been seen (Selmaoui et al, 1996) confirming earlier results (see Sienkiewicz et al, 1991; NIEHS, 1998; IARC, 2002).

Animal studies

55 Numerous animal studies have investigated the effects of exposure on carcinogenic processes. Overall, these studies provide no convincing evidence to support the hypothesis that exposure to magnetic fields can substantially increase the risk of cancer (AGNIR, 1994, 2001a; Boorman et al, 2000a,b; McCann et al, 2000; IARC, 2002). The most recent studies, in particular, are more extensive and generally have been carefully conducted, often using independent quality assurance procedures. These procedures were absent or less stringent in many of the earlier studies reporting either positive or negative effects.

56 A few animal studies have investigated the possibility that magnetic fields induce DNA damage. Increased DNA strand breaks have been reported in brain cells of exposed rodents (Lai and Singh, 1997a,b; Svedenstål et al, 1999a,b), but the results are inconclusive (IARC, 2002) and not supported by results from cellular studies.

57 Several recent large-scale studies have investigated the effects of continuous or intermittent lifetime exposure to magnetic fields on spontaneous tumour incidence in rats and mice (Mandeville et al, 1997; Yasui et al, 1997; Boorman et al, 1999; McCormick et al, 1999; NTP, 1999a). Results were negative with regard to leukaemia, brain cancer and mammary tumours. Although in one study the incidence of thyroid C-cell adenomas and carcinomas was elevated in male rats, this result might represent a chance event following multiple pair-wise comparisons (AGNIR, 2001a). Studies using transgenic mice (Eμ *pim-1* or TSG-*Trp53*) also reported no significant field induced effects on spontaneous lymphoma incidence (Harris et al, 1998; McCormick et al, 1998). In contrast, one study found a high increase in lymphoid hyperplasia and lymphoma in mice exposed over three generations to an intense 'travelling' magnetic field (Fam and Mikhail, 1996). However this study appears to have severe methodological and other flaws (Boorman et al, 2000a; McCann et al, 2000; AGNIR, 2001a; IARC, 2002).

58 Similarly, possible promotional or co-promotional effects of magnetic fields have been examined using a variety of multistage carcinogenesis models. Here the animals are treated with a carcinogen known to induce a particular cancer, and also exposed to various EMF intensities, sometimes in conjunction with a known promoting agent. Studies conducted through the 1990s have reported mainly negative results of magnetic fields using the classical mouse skin tumour model (McLean et al, 1991, 1995, 1997; Stuchly et al, 1992; Rannug et al, 1993a, 1994; Sasser et al, 1998; DiGiovanni et al, 1999). Another laboratory reported accelerated development of ultraviolet radiation (UVR) induced skin tumours in transgenic (K2) and normal mice (Kumlin et al, 1998a) and inhibition of UVR induced apoptosis in mouse skin (Kumlin et al, 2002). Other studies seeking evidence of promotional effects of magnetic fields on the incidence of lymphoma and other haemopoietic neoplasias have also reported a lack of field dependent effects using transgenic (*pim-1*) or normal mice (Shen et al, 1997; McCormick et al, 1998; Babbit et al, 2000; Heikkinen et al, 2001a). Lastly, no field dependent effects were seen on the induction of chemically induced pre-neoplastic foci in the rat liver (Rannug et al, 1993b,c). In addition, a few animal studies have investigated effects relevant to the non-genotoxic mechanisms of cancer, but the results are inconclusive (see also IARC, 2002). Changes in the activity of ornithine decarboxylase (ODC) have been reported in various tissues after short-term exposure of rodents to magnetic fields (Mevissen et al, 1995, 1999; Kumlin et al, 1998b) but not after longer exposure periods (Kumlin et al, 1998b; Sasser et al, 1998; Mevissen et al, 1999).

59 Rat mammary carcinomas represent a standard laboratory animal model in the study of human breast cancer. Several groups have investigated the possible promotional effects of magnetic fields on chemically induced mammary tumours in female rats following an earlier report that suggested long-term exposure increased incidence and malignancy of tumours (Beniashvili et al, 1991). In an extensive series of medium-term studies, Löscher, Mevissen and colleagues have reported that magnetic fields may increase tumour incidence, possibly due to field induced increases on tumour growth rate. Further, a significant linear correlation was found between increase in tumour incidence and magnetic flux density (Löscher and Mevissen, 1994, 1995; Löscher et al, 1993, 1994, 1998; Mevissen et al, 1993, 1996a,b, 1998a,b; Thun-Battersby et al, 1999; Löscher, 2001). There was, however, considerable variation between experiments reported by this group in the incidence of tumours in the unexposed control animals (possibly due to seasonal and other factors) which confounds interpretation of these data (AGNIR, 2001a). Another study (Fedrowitz et al, 2002) reported an increase in two cell proliferation markers (bromodeoxyuridine and Ki-67) in rat mammary gland. In contrast, two studies have reported a lack of an effect of magnetic fields on chemically induced mammary tumours. One extensive study, consisting of three large experiments, found no effects following an attempt to repeat and extend some of the positive effects reported by Löscher and Mevissen (Anderson et al, 1999, 2000; Boorman, 1999; NTP, 1999b). Sensitivity to detect field induced effects, however, was not optimal in two of these experiments (AGNIR, 2001a). Another study found no effects following intermittent magnetic field exposure (Ekström et al, 1998). Therefore the evidence for magnetic field effects on chemically induced mammary tumours in female rats is inconsistent (IARC, 2002). Finally, the limited evidence suggests magnetic fields do not cause promotion of neurogenic tumours. One study

reported no detectable effects of lifetime exposure following gamma-radiation induced brain tumours (Kharazi et al, 1999). Another very extensive study found no effects on central and peripheral nervous system tumours in female rats exposed transplacentally to a potent chemical carcinogen (Mandeville et al, 2000).

60 The few studies that have investigated the effect of magnetic fields on the growth of transplanted tumours in rats have not reported any field dependent effects. One study found no effect on the progression of large granular lymphocytic leukaemia (Sasser et al, 1996; Morris et al, 1999). Another found no effect on the progression of acute myeloid leukaemia (Devary et al, 2000).

61 The possibility that exposure to electric or magnetic fields may disrupt melatonin rhythms, and so increase the risk of cancer (Stevens, 1994; Stevens et al, 1997) has also received attention using animal models. Early studies using 60 Hz electric fields (Wilson et al, 1981, 1983, 1986; Reiter et al, 1988) suggested that exposure of rats caused a significant, if temporary, depression in pineal melatonin levels. The inability of later studies to reproduce this phenomenon (Sasser et al, 1991; Grota et al, 1994) suggests that the original positive results may be attributable to artefact or confounding (Brady and Reiter, 1993; Reiter, 1993). No effects on circulating melatonin levels were seen in male baboons following several weeks' exposure to combined 60 Hz electric and magnetic fields (Rogers et al, 1995a), although effects were noted in a preliminary study using an irregular and intermittent exposure schedule (Rogers et al, 1995b).

62 A series of experiments by Kato and colleagues (summarised by Kato and Shigemitsu, 1997) provided some evidence to suggest that subchronic exposure of rats to circularly polarised magnetic fields, but not elliptically or linearly polarised magnetic fields, may temporarily depress melatonin production and secretion (Kato et al, 1993, 1994a–c). Interpretation of these studies; however, is complicated by variability in the data between experiments and the frequent use of inappropriate controls (AGNIR, 2001a). It has been postulated that reductions in melatonin may produce concomitant increases in sex hormones. Accordingly, serum testosterone levels were also measured in one of these experiments, but without any field dependent effect being observed (Kato et al, 1994d). Other studies using rats have provided inconsistent and mostly negative evidence for magnetic field dependent changes in pineal function (Löscher et al, 1994, 1998; Selmaoui and Touitou, 1995; Bakos et al, 1995, 1997, 1999; Mevissen et al, 1996a,b, 1998a; John et al, 1998; Fedrowitz et al, 2002). Similar results have been observed using mice (McCormick et al, 1995; Heikkinen et al, 1999). Studies using Suffolk ewe lambs (Lee et al, 1993, 1995) and Djungarian hamsters (Yellon, 1994, 1996; Truong et al, 1996; Niehaus et al, 1997; Truong and Yellon, 1997; Yellon and Truong, 1998; Wilson et al, 1999) also provided no consistent evidence that exposure to power frequency magnetic fields can cause sustained disruptions in melatonin levels. One *ex vivo* study, however, suggested field dependent effects may occur. Brendel et al (2000) reported that melatonin production from isolated pineal glands of Djungarian hamsters, when stimulated by isoproterenol, was significantly suppressed by exposure to 16.67 or 50 Hz magnetic fields at 86 μT. AGNIR is currently undertaking a review of the effects of EMFs on melatonin.

63 Lastly, the possibility that exposure to electric or magnetic fields might affect the progression of tumours via some field induced change in the immune response has been investigated. Overall, there is little consistent evidence of any inhibitory effect of

exposure to power frequency fields on the various aspects of immune system function relevant to tumour suppression that have been examined. The few studies that have attempted to correlate possible field induced changes in tumour incidence with significant changes in immune function have not been successful (AGNIR, 2001a).

64 No effects were seen in mice with long-term continuous or intermittent exposure to magnetic fields using *in vivo* assays of T-lymphocyte mediated immune response to bacterial infection and antigen stimulation (House et al, 1996).

65 Studies using *in vitro* assays following long-term *in vivo* exposure to magnetic fields have also been conducted. Using rats, Mevissen et al (1996b, 1998b) reported a transient initial increase of spleen T-lymphocyte proliferation in rats after 2 weeks' exposure was followed by a decrease after 13 weeks. Murthy et al (1995) reported a decrease in peripheral blood B-lymphocyte mitogenic response in a pilot study with baboons exposed to electric and magnetic fields, but this effect was not reproduced in the main study using more intense fields.

66 A few studies have been carried out of natural killer (NK) cell function. Exposure to continuous or intermittent magnetic fields was reported to reduce spleen NK cell activity in female mice, but not in male mice, or in male or female rats (House et al, 1996; House and McCormick, 2000). This change in NK cell activity in female mice was not correlated with field induced changes in spontaneous tumour incidence (McCormick et al, 1999). In contrast, Tremblay et al (1996) reported that spleen NK cell activity was enhanced by magnetic field exposure in the same strain of rats used by House et al (1996) when compared with that of cage control animals but not of sham-exposed animals. Non-significant reductions in spleen and blood NK cell activity were reported in SENCAR mice treated with chemical carcinogens as part of a tumour co-promotion study (McLean et al, 1991). Increased numbers of exposed animals also showed enlarged spleens and extremely high blood mononuclear cell counts, suggestive of leukaemia (or lymphoma), although the evidence of immune system neoplasia appeared weak.

67 The activity in a subgroup of peritoneal macrophages was also investigated by Tremblay et al (1996). No effects of exposure were seen on two measures of macrophage activity (production of nitric oxide and tumour necrosis factor), although a third measure of macrophage activity (hydrogen peroxide release) showed a dose-dependent increase when compared with cage control animals. Comparison with sham-exposed animals only produced a significant effect at the higher levels of exposure. Finally, antibody (B-lymphocyte) cell activity in mice was not affected by exposure to power frequency or pulsed magnetic fields (House et al, 1996).

Cellular studies

68 Cellular studies have been used primarily to investigate possible mechanisms of interaction with EMFs. Compared with long-term animal studies, they are relatively inexpensive and rapid to perform, although this type of study is not generally taken alone as evidence of effects *in vivo* (AGNIR, 2001a).

69 Very many cellular studies have investigated the possibility that exposure to EMFs may induce biological changes that may be relevant to the causation or development of cancer. As with studies using animals, a wide variety of cell systems, tests and exposure conditions have been employed. While there have been reports of a few field

dependent effects, there is no clear evidence that exposure to magnetic fields of less than 0.1 mT can affect biological processes (NIEHS, 1998, 1999; AGNIR, 2001a). Further, the positive effects reported tend to be of small magnitude that questions their biological significance. Several comprehensive reviews and expert committees have reaffirmed that low level magnetic fields lack reliably observable genotoxic activity (McCann et al, 1993; Murphy et al, 1993; Lacy-Hulbert et al, 1998; NIEHS, 1998, 1999; AGNIR, 2001a).

70 Various studies have investigated the potential of EMFs to act as initiators of cancers. Several authors have indicated that exposure to either pulsed or continuous EMFs cannot directly bring about the transformation of cells in culture (Balcer-Kubiczek et al, 1996; Jacobson-Kram et al, 1997; Saffer et al, 1997) or negatively affect cellular immortalisation (Gamble et al, 1999; Miyakoshi et al, 2000a). In addition, studies using the Ames test to identify mutation in bacteria have not found any field dependent effects using magnetic fields (Nafziger et al, 1993; Tabrah et al, 1994; Suri et al, 1996) or pulsed electric fields and EMFs (Jacobson-Kram, 1997). In contrast, Miyakoshi et al (1996a, 1997) reported that exposure to very intense magnetic fields at 400 mT increased mutation at the *hrpt* gene locus in human MeWo cells, particularly during S-phase of the cell cycle. These mutations were suppressed by the action of a wild-type *p53* gene (Miyakoshi et al, 1997). There is also some evidence to suggest that the yield of mutations caused by exposure to ionising radiation may be enhanced by exposure to intense (500 μT and above) magnetic fields (Miyakoshi et al, 1999; Walleczek et al, 1999) but not by weaker fields (Ansari and Hei, 2000). However, preliminary results from an attempt to replicate these studies have not proved successful (Michael et al, 2004, and see Lloyd et al, in press). Although some data have suggested that magnetic fields may increase both single and double strand DNA breaks in rat brain cells exposed *in vivo* (Lai and Singh, 1997a), other studies have failed to find evidence for the induction of DNA breaks or effects on DNA repair in human or animal cells exposed to electric, magnetic or combined fields (Fairburn and O'Neil, 1994; Cantoni et al, 1995, 1996; Jacobson-Kram et al, 1997; McNamee et al, 2000; Hone et al, 2003). Several authors have used chromosomal damage as a measure of mutagenic potential. A few studies provided some evidence for small effects with magnetic fields (Nordenson et al, 1994; Yaguchi et al, 1999), although other studies failed to find any effect with either electric or magnetic fields (Antonopoulos et al, 1995; Galt et al, 1995; Jacobson-Kram et al, 1997). Other authors have reported mainly negative results using the micronucleus test (Scarfi et al, 1994; Paile et al, 1995; Lagroye and Poncy, 1997). An increase in micronucleus formation was reported in a human squamous cell carcinoma cell line but not in a human amniotic fluid cell line (Simko et al, 1998). In addition, Cho and Chung (2003) reported that exposure of human lymphocytes to a 60 Hz magnetic field at 0.8 mT increased the frequencies of micronuclei and sister chromatid exchanges induced by a chemical tumour initiator. Field exposure alone caused no cytogenetic changes.

71 Many other studies have investigated the potential of EMFs to act as promoting agents for cancers using a variety of approaches. Several studies have addressed the question as to whether magnetic fields have any direct effects on cell proliferation. Results are mixed. Most studies using magnetic fields have reported no effect (Fiorani et al, 1992; Cridland et al, 1996b, 1999; Reipert et al, 1996) or relatively small effects

(Fitzsimmons et al, 1992; Schimmelpfeng and Dertinger, 1993, 1997), although inhibition of proliferation has been seen (Nindl et al, 1997). Positive effects have also been reported (Antonopoulos et al, 1995), especially using pulsed electric fields (Sauer et al, 1997; Wartenberg et al, 1997). It has been suggested that EMFs may stimulate cellular differentiation without affecting proliferation (Hisenkamp et al, 1997; Landry et al, 1997), although this possibility has been challenged (Macleod and Collazo, 2000).

72 In contrast, a series of experiments suggests that 50 or 60 Hz magnetic fields may exert effects on cellular proliferation under very specific circumstances. It has been reported that exposure above a threshold of 0.2–1.2 μT may cause a small, but significant, inhibition of the antiproliferative action of melatonin (or tamoxifen) in several human cancer cell lines, especially MCF-7 breast cancer cells (Liburdy et al, 1993; Harland and Liburdy, 1997; Afzal and Liburdy, 1998; Harland et al, 1998; Liburdy and Levine, 1998; Blackman et al, 2001; Ishido et al, 2001). However, the robustness of the original effect has been queried (NIEHS, 1998).

73 A number of studies have also investigated the possibility that EMFs may affect intracellular calcium ion movements and thereby influence cell signalling pathways. There is some evidence that these effects may be produced in human Jurkat cells using magnetic fields of a few millitesla, but they appear to depend critically on the state of the cells and their environment (Walleczek et al, 1994; Galvanovskis et al, 1996). Changes in calcium have been reported using weaker fields of 40–150 μT (Lindström et al, 1993, 1995a,b) but these results could not be replicated (Wey et al, 2000). Studies using magnetic fields tuned to postulated resonant conditions have not found effects (Prasad et al, 1991; Coulton and Barker, 1993; Lyle et al, 1997).

74 In addition, field dependent effects on other signalling pathways have been reported using a variety of models and exposure conditions. The most convincing evidence relates to changes on the SRC family kinase LYN (Uckun et al, 1995; Dibirdik et al, 1998), but increased production of superoxide anion O_2^- and β-glucuronidase (Khadir et al, 1999), and changes in PI3 kinase (Clejan et al, 1995; Santoro et al, 1997) have been seen. In contrast, Miller et al (1999) found no effect on the signalling pathways controlling the expression of the transcription factors NF-kB or AP-1.

75 Many studies have investigated possible field dependent effects on both general and specific gene expression. While early studies reported short-term increases in gross transcription (reviewed by NIEHS, 1998; AGNIR, 2001a), a more recent, well-performed study using 2 mT, 60 Hz magnetic fields found no evidence of differential expression of any of a very large number of genes (Balcer-Kubiczek et al, 1998).

76 Similarly, the results concerning the effects of EMFs on specific gene expression are inconsistent. Generally, the magnitude of any changes seen in the more reliable studies tend to be very small compared with those produced by known causative agents (such as growth factors or serum), whereas some of the studies reporting larger changes can be criticised for methodological flaws (Cridland et al, 1996a; AGNIR, 2001a). Some studies suggest that magnetic fields of 100 μT or more may affect the expression of *c-myc*, *c-fos*, and other regulatory genes (Phillips et al, 1992; Gold et al, 1994; Goodman et al, 1994; Lagroye and Poncy, 1998; Tuinstra et al, 1998) perhaps within frequency, time and field strength windows. However, the results are difficult to interpret because the studies have used a wide range of exposure conditions and cell types. Other studies suggest effects on heat shock and stress proteins (Goodman et al, 1994; Pipkin et al,

1999; Junkersdorf et al, 2000; Miyakoshi et al, 2000b) again using intense fields. In contrast, many studies have not reported any effects on *c-myc* expression and other proto-oncogenes (Parker and Winters, 1992; Greene et al, 1993; Reipert et al, 1994; Desjobert et al, 1995; Miyakoshi et al, 1996b; Harrison et al, 1997; Jahreis et al, 1998; Loberg et al, 1999). In particular, two very-well-performed studies did not detect any field dependent increases in gene expression (Lacy-Hulbert et al, 1995; Saffer and Thurston, 1995). Another well-conducted series of experiments found no field dependent effect on the genes directly involved in cell cycle control (Dees et al, 1996).

77 Given the possibility that magnetic fields may affect intracellular calcium ion movements, a few studies have sought to determine whether electric fields applied to the cultures can affect gene expression. Modest changes were seen in *c-myc*, histone H2B and *hsp70* genes in HL-60 cells exposed at 0.3–3 V m^{-1} (Blank and Soo, 1992; Goodman et al, 1994) and in *c-fos* expression in prostate tumour spheroids following exposure to a single pulse at 500 V m^{-1} (Sauer et al, 1997).

78 Lastly, recent attempts to replicate or extend the results of Litovitz et al (1991) regarding magnetic field induced stimulation of basal ornithine decarboxylase (ODC) activity failed to find any evidence for effects on ODC expression (Azadniv et al, 1995; Balcer-Kubiczek et al, 1996; Cress et al, 1999).

The carcinogenic potential of low frequency magnetic fields has been investigated in laboratories using a wide range of models and endpoints.

From the results of this research there is no convincing evidence to suggest that magnetic fields are directly genotoxic or that they can bring about the transformation of cells in culture. They are therefore unlikely to initiate carcinogenesis.

Some cellular studies report possible enhancement of genetic change caused by known genotoxic agents; effects on intracellular signalling, especially calcium flux; and effects on specific gene expression. Many of these positive effects involve magnetic flux densities greater than 0.1 mT or induced electric field strengths greater than about 1 mV m^{-1}.

However, results from different studies are often contradictory and there is an almost total failure of independent replication of positive results. Those results that report a positive effect tend to show only small changes, the biological consequences of which are not clear.

The results of animal studies do not suggest that magnetic fields can cause cancer or affect its development.

A large number of well-conducted, good quality studies have not shown any field dependent effects using a range of tumour models, although the possibility that exposure may affect chemically induced mammary tumours cannot be dismissed.

The lack of a natural animal model of the most common form of childhood leukaemia, acute lymphoblastic leukaemia, and similarly of spontaneous brain tumour, are potential shortcomings of these data.

Laboratory studies with volunteers do not suggest that melatonin rhythms are affected by acute night-time exposure to magnetic fields. However, the possibility that changes in melatonin physiology may occur in sensitive subgroups, and perhaps following prolonged exposure, cannot be ruled out.

The carcinogenic potential of low frequency electric fields has not been experimentally investigated and cannot be determined.

Reproduction and development

79 Interest has been expressed in the possibility that exposure to low frequency EMFs may affect fertility, reproduction or prenatal and postnatal growth and development. This issue has been addressed using both mammals and birds; however, the results of studies using mammals are more relevant to possible effects on humans. Several comprehensive reviews are available (Brent et al, 1993; AGNIR, 1994; Juutilainen and Lang, 1997; Huuskonen et al, 1998a; NIEHS, 1998; Brent, 1999; IARC, 2002; Juutilainen, 2003; ICNIRP, 2004).

Animal studies

80 No recent studies appear to have explored the reproductive and developmental effects of low frequency electric fields. Earlier studies using rats, mice and miniature swine (reviewed by AGNIR, 1994; NIEHS, 1998; IARC, 2002; ICNIRP, 2004) indicated that even intense and chronic exposure over several generations caused no consistent adverse effects, once the confounding effects of spark discharge had been eliminated.

81 The possible effects of magnetic fields have received much attention. One recent study assessed the effects of a range of 60 Hz fields on fertility and reproductive performance in rats over three generations (Ryan et al, 1999). No field dependent toxicity was observed; fetal viability and body weight were similar in all groups, and there were no differences between test and control groups in any measure of reproductive performance (number of litters per breeding pair, percentage of fertile pairs, latency to parturition, litter size or sex ratio). Similarly, medium-term exposure of mice to 50 Hz magnetic fields at 25 μT before mating produced no effects on fertility (Elbetieha et al, 2002), although fertility was reduced in rats exposed under the same conditions (Al-Akhras et al, 2001). Also a single 4-hour exposure of hybrid male mice to a magnetic field at 1.7 mT was reported to decrease numbers of elongated spermatids at 28 days after exposure (De Vita et al, 1995). No effects were observed at earlier or later time points, or using an exposure time of 2 hours.

82 Other recent studies using rodents have indicated that exposure to sinusoidal power frequency magnetic fields or saw-tooth fields for either a part or the whole of gestation caused no obvious adverse effects. Early exposure of rats or mice to 50 Hz fields was without consistent effect on embryo implantation and vitality (Huuskonen et al, 2001a,b). However, some differences in estrogen-receptor and progesterone-receptor densities at some time points were observed in the rat uterus. Several well-designed studies noted an increase in the incidence of minor skeletal variants following *in utero* exposure to power frequency fields up to 30 mT or saw-tooth fields at up to 15 μT (peak-to-peak) (Huuskonen et al, 1993, 1998b; Kowalczuk et al, 1994; Mevissen et al, 1994; Ryan et al, 2000), although other studies have not reported this effect (Rommereim et al, 1996; Ryan et al, 1996). In these studies overall, exposure was without any significant detrimental effect on fetal development or maternal toxicity.

83 Although results obtained using avian species are not useful for predicting reproductive effects in humans (Brent, 1999), the effects of exposure to pulsed and sinusoidal magnetic fields have been investigated using chicken and quail embryos (eggs). As with earlier studies that were broadly supportive of a field induced increase in abnormalities (see AGNIR, 1994; ICNIRP, 2004), some recent studies have reported

field dependent effects (Terol and Panchon, 1995; Farrell et al, 1997) whereas other studies have not (Cox et al, 1993). It has also been reported that 50 Hz magnetic fields at 10 mT may modify the embryotoxic effects of x-rays and chemical teratogens (Pafková and Jerábek, 1994; Pafková et al, 1996). Exposure to the magnetic field before treatment reduced embryonic death and malformations, while embryotoxicity was increased when the magnetic field followed the x-ray exposure. Finally, a few recent studies have investigated the effects of magnetic fields on other non-mammalian embryos. No malformations were seen using zebrafish embryos (Skauli et al, 2000) and no consistent changes were reported using *Drosophila* (Nguyen et al, 1995; Graham et al, 2000).

84 Behavioural teratology represents a sensitive approach to assess the impact of potential neurotoxic agents (Lovely, 1988). A number of subtle effects on developmental indices and landmarks have been reported in different studies, but, overall, no evidence to suggest a consistent pattern of deficits is apparent in recent studies using rats or mice exposed to magnetic fields (Sakamoto et al, 1993; Sienkiewicz et al, 1994, 1996a). Prenatal exposure to combined electric and magnetic fields had no consistent effect on somatic growth and cerebral development in rats (Yu et al, 1993), whereas postnatal exposure was reported to cause transient changes in brain weight and in the concentrations of DNA and RNA in the cerebellum (Gona et al, 1993).

There is only weak evidence to suggest that low frequency electric or magnetic fields can adversely affect fertility, reproduction or development in mammals. Subtle changes in skeletal anomalies and on postnatal landmarks have sometimes been observed but there is little consistency in the data overall.

Neurobehavioural effects

85 The brain and nervous systems function by using electrical signals, and may therefore be considered particularly vulnerable to low frequency EMFs and the resultant induced electric currents. Substantial numbers of laboratory experiments with volunteers and animals have investigated the possible consequences of exposure to weak EMFs on various aspects of nervous system function, including cognitive, behavioural and neuroendocrine changes. These studies have been reviewed by NRC (1997), NIEHS (1998), IARC (2002) and ICNIRP (2004). In general, very few effects have been established, and even the more robust field induced responses tend to be small in magnitude, subtle and transitory (Sienkiewicz et al, 1993; Crasson et al, 1999).

Volunteer studies

86 Studies of people have investigated a wide range of possible field induced effects on brain function and behaviour. These include effects on cognition, the electroencephalogram (EEG), as well as effects on sleep, and the control of heart rate. The possibilities of electrical hypersensitivity and field induced effects on mood have also been investigated. Effects on melatonin rhythms are considered in paragraphs 49–78 on cancer. The effects induced by intense exposure to EMFs above the threshold for perception have been considered in paragraphs 33–42 on acute electrophysiological responses.

87 *Cognitive studies* Despite the potential importance of field induced effects on attention, vigilance, memory and other information processing functions, relatively few studies have looked for evidence of changes in cognitive ability during or after exposure to low frequency EMFs. These have been reviewed by NIEHS (1998) and Cook et al (2002). While few field dependent changes have been observed, it is important to consider that this type of study may be particularly susceptible to various environmental and individual factors which may increase the variance of the experimental endpoint and decrease the power to detect a small effect. This may be particularly important, since any field dependent effects are likely to be small with fields at environmental levels (Sienkiewicz et al, 1993; Whittington et al, 1996).

88 The effects of acute exposure to magnetic fields on simple and choice reaction time have been investigated in several recent studies using a wide range of magnetic flux densities (20 μT – 1.26 mT) and experimental conditions. Most studies have not found any field dependent effects (Gamberale et al, 1989; Cook et al, 1992; Lyskov et al, 1993a,b; Podd et al, 1995, 2002; Preece et al, 1998), although modest effects on speed (Graham et al, 1994; Whittington et al, 1996; Crasson et al, 1999) and accuracy during task performance (Cook et al, 1992; Kazantzis et al, 1996; Preece et al, 1998) have been reported. These data also suggest that effects may depend on the difficulty of the task (Kazantzis et al, 1996; Whittington et al, 1996) and that exposure may attenuate the usual practice effects on reaction time (Lyskov et al, 1993a,b; Stollery, 1986).

89 A few studies have reported subtle field dependent changes in other cognitive functions, including memory and attention (see also Cook et al, 2002). Using a battery of neuropsychological tests, Preece et al (1998) found that exposure to a 50 Hz magnetic field at 0.6 mT decreased accuracy in the performance of a numerical working memory task and decreased sensitivity in the performance of a word recognition task. Similarly, Keetley et al (2001) investigated the effects of exposure to 28 μT, 50 Hz fields using a series of cognitive tests. A significant decrease in performance was seen with one working memory task (the trail-making test, part B) that involves visual-motor tracking and information processing within the prefrontal and parietal areas of the cortex. Podd et al (2002) reported delayed deficits in the performance of a recognition memory task following exposure to a 50 Hz field at 100 μT. Trimmel and Schweiger (1998) investigated the effects of acute exposure to 50 Hz magnetic fields at 1 mT. The fields were produced using a power transformer, and volunteers were exposed in the presence of a 45 dB sound pressure level noise. Compared with a no-field, no-noise condition and noise alone (generated using a tape recording) significant reductions in visual attention, perception and verbal memory performance were observed during field exposure. The presence of the noise during exposure, however, complicates interpretation of this study.

90 *Electrical activity of the brain* Since the first suggestion that occupational exposure to EMFs resulted in clinical changes in the electroencephalogram (EEG) was published in 1966, various studies have investigated if exposure to magnetic fields can affect the electrical activity of the brain. Such methods can provide useful diagnostic information regarding the functional state of the brain, not only from recordings of the spontaneous activity at rest but also from recording the sensory

functions and subsequent cognitive processes evoked in response to specific stimuli (evoked or event-related potentials). Nevertheless, neurophysiological studies using magnetic fields need to be performed with much care and attention since they can be prone to many potential sources of error and artefact (NIEHS, 1998). Changes in arousal and attention of volunteers, in particular, can substantially affect the outcome of these studies.

91 Various studies have investigated the effects of magnetic fields on brain activity by analysing the spectral power of the main frequency bands of the EEG (Silny, 1986; Gamberale et al, 1989; Bell et al, 1991, 1992, 1994a,b; Lyskov et al, 1993a; Marino et al, 1996; Schienle et al, 1996; Heusser et al, 1997). These studies have used a wide variety of experimental designs and exposure conditions, as well as healthy volunteers and patients with neurological conditions, and thus are difficult to compare and evaluate. Despite some scattered field dependent changes, most notably in the alpha frequency band, and with intermittent exposure perhaps more effective than continuous exposure, these studies have produced inconsistent and sometimes contradictory results. Nevertheless these possibilities cannot be dismissed, although replicable field dependent effects seem unlikely.

92 Other studies have investigated the effects of magnetic fields and combined electric and magnetic fields on evoked potentials within the EEG waveform. There are some differences between studies, but generally, the early components of the evoked response corresponding to sensory function do not appear affected by exposure (Lyskov et al, 1993b; Graham et al, 1999). In contrast, large and sustained changes on a later component of the waveform (N100) representing stimulus detection may be engendered by intense exposure at 60 mT (Silny, 1984, 1985, 1986), with lesser effects occurring using fields at 1.26 mT (Lyskov et al, 1993b), and nothing below 30 μT (Graham et al, 1999). Finally, exposure during the performance of some discrimination and attention tasks may affect the late major components of the EEG (around P300) which are believed to reflect cognitive processes involved with stimulus evaluation and decision making (Cook et al, 1992; Graham et al, 1994; Crasson et al, 1999; see also Sartucci et al, 1997). There also is some evidence that task difficulty and field intermittency may be important experimental variables. However, all these subtle effects are not well defined, and some inconsistencies between studies require additional investigation and explanation.

93 *Sleep* The possibility that EMFs may exert a detrimental effect on sleep has been examined in two studies. Using the EEG to assess sleep parameters, Åkerstedt et al (1999) reported that continuous exposure of healthy volunteers to a 50 Hz at 1 μT at night caused slight disturbances in sleep. In this study, total sleep time, sleep efficiency, slow-wave sleep (stage III and IV), and slow wave activity were significantly reduced by exposure, as was subjective depth of sleep. Graham and Cook (1999) reported that intermittent, but not continuous, exposure to 60 Hz, 28 μT magnetic fields at night resulted in less total sleep time, reduced sleep efficiency, increased time in stage II sleep, decreased time in rapid eye movement (REM) sleep, and increased latency to first REM period. Consistent with a pattern of poor and broken sleep, volunteers exposed to the intermittent field also reported sleeping less well and feeling less rested in the morning.

94 *Hypersensitivity and mood states* It has been suggested that some individuals display increased sensitivity to EMFs. People self-reporting hypersensitivity may experience a wide range of severe and debilitating symptoms, including sleep disturbances, general fatigue, difficulty in concentrating, dizziness, and eyestrain. In extreme forms, everyday living may become problematical. A number of skin problems such as eczema and sensations of itching and burning have also been reported, especially on the face, and, although there may be no specific symptom profile (see Hillert et al, 2002), increased sensitivity to chemical and other factors often occurs (Levallois et al, 2002). The responses to EMFs are reported to occur at field strengths orders of magnitude below those required for conventional perception of the field (Silny, 1999). Bergqvist and Vogel (1997), Levallois (2002) and ICNIRP (2004) have reviewed these data.

95 In contrast to anecdotal reports, the evidence from double-blind provocation studies (Andersson et al, 1996; Arnetz, 1997; Arnetz et al, 1997; Sandström et al, 1997; Flodin et al, 2000; Lonne-Rahm et al, 2000; Lyskov et al, 2001a) indicates that neither healthy volunteers nor self-reporting hypersensitives can reliably distinguish field exposure from sham-exposure. In addition, subjective symptoms and circulating levels of stress-related hormones and inflammatory mediators could not be related to field exposure. Not all studies dismiss the possibility, however. Two studies have reported weak positive field discrimination (Rea et al, 1991; Mueller et al, 2002) and another study reported subtle differences in heart rate and electrodermal activity between normal and hypersensitive volunteers (Lyskov et al, 2001b). There is some morphological evidence to suggest that the numbers and distribution of mast cells in the dermis of the skin on the face may be increased in individuals displaying hypersensitive reactions (Johansson et al, 1994, 1996; Gangi and Johansson, 2000). Increased responsiveness was attributed to changes in the expression of histamine and somatostatin and other inflammatory peptides. Similar effects in the dermis have also been reported following provocation tests to VDU-type fields in normal, healthy volunteers (Johansson et al, 2001). The possibility that hypersensitivity may be associated with enhanced ability to perceive electric currents has been suggested by Leitgeb and Schröttner (2003).

96 The possible impact of EMFs on mood and arousal has also been assessed in double-blind studies in which volunteers completed mood checklists before and after exposure. No field dependent effects have been reported using a range of field conditions (Maresh et al, 1988; Cook et al, 1992; Graham et al, 1994; Selmaoui et al, 1997; Crasson et al, 1999). In contrast, Stollery (1986) reported decreased arousal in one of two participating groups of subjects when mild (500 μA) 50 Hz electric current was passed through the head, upper arms, and feet. This was done to simulate the internal electric fields generated by exposure to an external electric field strength of 36 kV m^{-1}. Also Stevens (2001) reported that exposure to a 20 Hz, 50 μT magnetic field increased positive affective responses displayed to visual stimuli compared with sham-exposure. Arousal, as measured by skin conductance, gave variable results.

97 *Effects on cardiac activity* Studies of the effects of EMFs on field induced changes in autonomic control of the heart have produced inconclusive results. Although EMFs appear to have no effect on the electrical activity of the heart (Silny, 1981), a series of studies from the US Midwest Research Institute have suggested a small (3–5 beats per

minute, bpm), but significant reduction in mean heart rate may occur during and immediately after exposure to 60 Hz electric and magnetic fields at 9 kV m^{-1} and 20 μT (Cook et al, 1992; Graham et al, 1994). This response did not occur with exposure to stronger or weaker fields, and was reduced if the subject was mentally alert, or following fairly hard exercise when heart rate was elevated (Maresh et al, 1988; Graham et al, 1990). There were no other consistent effects on a wide battery of sensory and perceptual tasks. NIEHS (1998) commented that the magnitude of the observed effect was comparatively small and the biological mechanism underlying the phenomenon had not been identified. Based on an analysis of cardiac cellular electrophysiology, Cooper et al (2003) concluded that it was highly unlikely that exposure to ELF fields at environmental levels could cause direct effects on the heart.

98 In independent studies, no effects on heart rate or blood pressure were seen during day-time exposure to 50 Hz fields at 0.1–10 kV m^{-1} and 1–15 μT for up to a few hours (Korpinen et al, 1993; Korpinen and Partanen, 1994a,b, 1996) or at 100 μT for 9 minutes (Whittington et al, 1996).

99 More recently, a change in heart rate variability (HRV) in healthy young men was found during night-time exposure to an intermittent 60 Hz magnetic field at 20 μT (Sastre et al, 1998) or a 16 Hz field at 28 μT (Sastre et al, 2000). HRV results from the action of various neuronal and cardiovascular reflexes and is correlated with sleep stage. Continuous exposure or exposure at 1 μT had no effect on HRV. Similar responses were reported in older men, but not women, exposed to 60 Hz fields at 28 μT (Graham et al, 2000b). However, no effects were reported in two subsequent studies using intermittent exposure to 60 Hz fields at either 28 μT (Graham et al, 2000c) or 127 μT (Graham et al, 2000d).

100 In order to clarify these data, a pooled analysis of these studies was carried out (Graham et al, 2000e). This indicated that the changes in HRV were observed only in studies where blood sampling had taken place using an implanted catheter. It was suggested that these procedures might have altered the arousal of the subjects, which disturbed their sleep and thus affected HRV. This analysis also failed to identify either magnetic flux density or exposure pattern as a main factor.

Animal studies

101 Various animal models have been used to investigate possible field induced effects on brain function and behaviour. These include effects on neurotransmitter levels, electrical activity, field detection and the performance of learned tasks. Other studies have investigated effects on melatonin rhythms and these are considered in paragraphs 49–78 on cancer. Overall, a few field dependent responses have been tentatively identified but even the most consistent effects appear small in magnitude and transient in nature.

102 *Neurotransmitter function* A number of studies have investigated the potential of low frequency fields to affect the levels of different neurotransmitters within various regions of the brain. These data have been most recently reviewed by ICNIRP (2004).

103 Early studies reported effects of both acute and chronic exposure to intense electric fields on catecholamine and amino acid neurotransmitter levels in some parts of the brain, but values often stayed within the normal range.

104 More recently, Margonato et al (1995) reported that chronic exposure to 50 Hz magnetic fields at 5 μT had no effect on levels of norepinephrine, dopamine and its major metabolites, or 5-hydroxytrytamine or its major metabolite in the striatum, hypothalamus, hippocampus or cerebellum. In a companion study, Zecca et al (1998) reported a similar lack of effects following chronic exposure to combined electric and magnetic fields at either 1 kV m^{-1} and 5 μT or 5 kV m^{-1} and 100 μT. However, intensity-dependent changes were reported in the opioid system in the frontal cortex, parietal cortex and hippocampus, but not in other brain areas investigated.

105 Other studies have also investigated field dependent changes in opioid-related physiology. In a series of related experiments, Kavaliers, Prato and colleagues have indicated that various types of low frequency magnetic field may affect the endogenous opioid systems and modulate the response of animals to the analgesic effects of injected opiates such as morphine (reviewed by Kavaliers et al, 1994). These responses are complex, and magnetic fields appear to have a differential effect on the functions of different opioid receptor subtypes (Kavaliers and Ossenkopp, 1991). There is also evidence that the mechanism for these effects may involve changes in calcium ion channel function (Kavaliers et al, 1998a) protein kinase C (Kavaliers et al, 1991) and nitric oxide (NO) production and NO synthase activity (Kavaliers et al, 1998b). Recent studies with land snails suggest the field induced analgesic effects depend on the relative direction of the applied fields (Prato et al, 1995) as well as the presence of light (Prato et al, 1996, 1997, 2000).

106 In another series of experiments, it was reported that the acute exposure of rats to a 60 Hz magnetic field at 0.75 mT decreased activity in the cholinergic pathways in the frontal cortex and hippocampus (Lai et al, 1993). These effects were blocked by naltrexone, but not by naloxone, which was taken as evidence that magnetic fields affected endogenous opioids only within the CNS. Further studies showed the changes in cholinergic activity appeared to be mediated by activation of endogenous opioids (Lai and Carino, 1998). There also appears to be some interaction between exposure duration and field intensity, such that longer exposures (3 hours) at lower intensity fields (0.05 mT) could induce changes in cholinergic activity (Lai and Carino, 1999).

107 Several authors have investigated the possibility that prior field exposure might alter electrical activity in the brain and thus influence the onset or severity of epileptic seizures induced in rats by electrical or chemical stimulation or by a loud noise. Generally, the effects that have been reported are consistent with a reduction in susceptibility to epileptic seizure but are inconsistent between different studies (ICNIRP, 2004). Recently, Potschka et al (1998) reported that chronic exposure to 50 Hz magnetic fields of 100 μT exerted weak inhibitory effects on some seizure parameters of the kindling model with exposed rats showing a higher threshold for generalised seizures.

108 *Electrical activity* A number of animal studies have investigated if acute exposure to low frequency electric and magnetic fields can affect brain electrical activity as measured as the EEG or as evoked potentials following presentation of a sensory stimulus (reviewed by Sienkiewicz et al, 1991; NIEHS, 1998). The results of these studies are somewhat mixed and difficult to interpret, but none suggests any obvious adverse health effect (ICNIRP, 2004). Some of these studies may have been confounded by

experimental design or artefact – it has long been recognised that recording potentials through electrodes attached to the skull is liable to artefact in the presence of EMFs. Two more recent studies reported significant EEG changes in rabbits during magnetic field exposure (Bell et al, 1992) and in rats following magnetic field exposure (Lyskov et al, 1993a). However, the possibility of artefact or of false positive results complicates interpretation of both studies (NIEHS, 1998).

109 *Field detection* It is known that animals can detect the presence of low frequency electric fields, possibly as a result of surface charge effects (Weigel et al, 1987; although see Stell et al, 1993). Using appropriate behavioural techniques, a number of studies using rats (reviewed by NRC, 1997; NIEHS, 1998) indicate that the threshold for field detection is about 3–13 $kV\,m^{-1}$. Detection thresholds are similar in a variety of other species, with thresholds reported at 5–12 $kV\,m^{-1}$ in baboons (Orr et al, 1995a), 25 $kV\,m^{-1}$ in mice, and 35 $kV\,m^{-1}$ in birds and miniature swine.

110 Detection thresholds for magnetic fields in animals are less clear and show greater variability than those for electric fields (ICNIRP, 2004). Using a conditioned suppression paradigm, Smith et al (1994) reported that rats were able to detect ELF magnetic fields as low as 200 μT, although the validity of this result has been questioned by Stern and Justensen (1995).

111 *Arousal and aversion* Initial exposure to power frequency electric fields in excess of detection thresholds may cause transient arousal and stress responses in rodents and non-human primates (IARC, 2002). These responses appear to habituate quickly following prolonged exposure. There is also some evidence that animals may avoid exposure to intense electric fields, although the strength of this unconditioned response is too weak to elicit aversive behaviours (Creim et al, 1984; Rogers et al, 1995a). Thus electric fields at levels of up to 65 $kV\,m^{-1}$ are not considered to be highly aversive to non-human primates.

112 Exposure of baboons to combined 60 Hz electric and magnetic fields at 6 $kV\,m^{-1}$ and 50 μT or at 30 $kV\,m^{-1}$ and 100 μT did not produce significant changes in social behaviour (Coehlo et al, 1995) previously seen to be affected by exposure to electric fields alone (Coehlo et al, 1991; Easley et al, 1991). While it is possible that the magnetic field may have modulated the electric field induced responses, it was considered that some of the animals in the later experiment may have become desensitised by prior subthreshold electric field exposure.

113 Acute exposure to power frequency magnetic fields at up to a few millitesla does not appear to induce aversive behaviour (Lovely et al, 1992; IARC, 2002). Such results suggest that the arousal responses observed using electric fields are not caused by field induced internal electric fields, and may be attributed to body-surface interactions. One study reported that long-term, intermittent exposure to 50 Hz at 18 mT reduced behavioural responses ('irritability') induced by tactile and somatosensory stimuli in rats (Trzeciak et al, 1993). Another study reported that exposure to specific combinations of static and low frequency fields affected exploratory behaviour in rats (Zhadin et al, 1999). Exposure to conditions corresponding to the putative cyclotron resonance for calcium ions reduced this behaviour, and exposure to such conditions for magnesium ions increased it.

114 *Learned tasks* Early studies with macaque monkeys reported that exposure to low frequency electric fields at well below detection thresholds may affect operant performance – see IARC (2002). However, more recent, well-conducted studies using baboons found exposure to 60 Hz electric fields at 30 and 60 kV m^{-1} had no sustained effect on the performance of two operant schedules (Rogers et al, 1995a,b), although initial exposure may contribute towards producing a temporary interruption in responding.

115 Similarly, studies using 60 Hz electric and magnetic fields (Orr et al, 1995b) indicated that combined exposure to 6 kV m^{-1} and 50 μT or to 30 kV m^{-1} and 100 μT had no effect on operant performance on a delayed match-to-sample task in baboons. This result is generally consistent with earlier results from other research groups using non-human primates (reviewed by Sienkiewicz et al, 1991; NIEHS, 1998). However, one study using rats (Salzinger et al, 1990) suggested exposure to 60 Hz fields of 30 kV m^{-1} and 100 μT may exert subtle effects on performance that depend on the time of testing within the light–dark cycle.

116 Several recent studies using the Morris water maze or radial arm maze have investigated the effects of magnetic fields on spatial memory and place learning. These studies provide evidence that exposure of rats, mice or voles to power frequency fields at 100 μT and above may modulate task performance (Kavaliers et al, 1993, 1996; Lai, 1996; Lai et al, 1998; Sienkiewicz et al, 1998a,b). Exposure to complex pulsed magnetic fields may also affect performance (Thomas and Persinger, 1997; McKay and Persinger, 2000). In addition, much evidence has accrued over the last decade (but is still only available from presentations at scientific meetings) that effects may also occur using specific combinations of static and time-varying fields (see Sienkiewicz et al, 1998b). The mechanism for these effects has been partly explored and the changes in behaviour have been attributed to decreases in cholinergic functions caused by field induced changes in endogenous opioid activity (Lai, 1996; Thomas and Persinger, 1997; Lai and Carino, 1998). How the magnetic field may have activated the endogenous opioid systems is not known.

117 The conditions to produce any of these phenomena are not well defined, and both deficits and enhancements in performance have been observed and one study did not report any field dependent effects (Sienkiewicz et al, 1996b). It is feasible that these differences in outcome may depend on experimental or other variables including the timing and duration of exposure relative to learning (McKay and Persinger, 2000; Sienkiewicz et al, 2001). While these results suggest that the neural representations or processes underlying the performance of spatial memory tasks may be vulnerable to the effects of magnetic fields, some part of the observed outcome may be attributable to changes in arousal (IARC, 2002) or in motivation (Thomas and Persinger, 1997). Nevertheless, the transient nature and small magnitudes of the responses do not suggest an obvious deleterious effect.

118 Two studies using rodents have investigated the effects of magnetic fields on recognition memory. Using the field conditions putatively identified as having an acute effect of spatial memory, Sienkiewicz et al (2001) found no effects on the performance of an object recognition task by mice. Animals were exposed for 45 minutes to a 50 Hz field at 7.5, 75 or 750 μT. However, Mostafa et al (2002) reported that discrimination

between familiar and novel objects was impaired in rats following chronic exposure at 200 μT for 2 weeks.

119 Stern et al (1996) failed to replicate the results of earlier studies (Thomas et al, 1986; Liboff et al, 1989) suggesting exposure to combined static and power frequency magnetic fields – arranged to simulate the cyclotron resonance conditions for lithium ions – significantly impaired operant performance. The earlier positive results were attributed to possible confounding.

The possibility that exposure to low frequency EMFs may affect neurobehavioral function has been explored in humans and animal models using a range of exposure conditions. Few robust effects have been established.

Studies with volunteers exposed to low intensity magnetic fields have produced only evidence of subtle and transitory effects. Generally, the conditions necessary to elicit these responses are not well defined at present.

There is some evidence suggesting field dependent effects on reaction time and reduced accuracy in performance of some cognitive tasks, which is supported by the results of studies on the EEG.

Other possible field dependent changes are less well defined. Studies investigating effects on sleep quality have reported inconsistent results. It is possible that these differences may be attributable in part to differences in design between studies.

Mild changes in cardiac activity have been reported from one laboratory, but only under highly specific exposure conditions. These changes have not been independently replicated.

The phenomenon of electromagnetic hypersensitivity has been reported in some people. However, the suggestion from double blind trials is that the reported symptoms are unrelated to EMF exposure.

There is convincing evidence that power frequency electric fields can be detected by animals, most likely as a result of surface charge effects. Exposure above the detection threshold of about 5–15 kV m^{-1} may induce transient arousal or mild stress, but fields are not considered aversive, even at high field strengths.

Other possible field dependent changes in animals are less well defined and generally laboratory studies have produced evidence of only subtle and transitory effects.

There is evidence that exposure to magnetic fields may modulate the functions of the opioid and cholinergic systems, and this is supported by the results of studies investigating effects on analgesia and on the acquisition and performance of spatial memory tasks.

Biological uncertainties

120 The perceptual and sometimes painful effects of surface charge are well understood. Laboratory evidence shows the distribution of sensitivity in volunteers, but quantitative published data are lacking on the occurrence and severity of these effects in workers and members of the public in the UK.

121 Thresholds for peripheral nerve stimulation by induced electric fields are well understood; data are accumulating concerning brain tissue stimulation thresholds. The effects of weak electric fields on nervous tissue, at levels below the threshold

for direct stimulation, have been explored *in vitro* but their possible consequences *in vivo* are less well understood. It may be expected that functions of electrically excitable nerve and muscle tissue that show network behaviour, particularly the CNS, will be altered by relatively weak fields, but these probable effects need further experimental investigation.

122 Recommendations on limiting exposure to low frequency EMFs can be based on an extrapolation of phosphene and other physiological data concerning brain tissue electrophysiology. Magnetic and electric phosphenes clearly result from interaction of the induced field with electrically sensitive cells that comprise the neuronal circuitry of the retina; the threshold and frequency response has been studied in several laboratories. The retinal circuitry has been taken as a sensitive model of neuronal circuitry in other parts of the brain. However, the effects of weak electric fields on, for example, cognitive processes, have not been clearly demonstrated *in vivo*, nor have thresholds and their variation with frequency been clearly defined.

123 The results of many of the other studies suggesting that low level, low frequency EMFs may induce adverse biological responses are beset with uncertainty over their interpretation, limiting their practical usefulness as a basis for establishing exposure standards. This uncertainty originates from several sources. Firstly, many of these studies were performed with inadequate scientific rigour, namely, poor experimental design, insufficient control of potential artefacts, and inadequate dosimetry and metrology. Other studies may have inappropriate or incorrect data analysis or have insufficient statistical power to detect small effects.

124 Another source of uncertainty results from the inconsistency in reported effects (both within and between laboratories) and from the general lack of attempts to confirm or replicate reported results. This is as true for studies reporting the absence of effects as for those reporting the presence of field dependent effects. Many of the experimental data consist of isolated observations where there have been few attempts to integrate results between different experiments and experimental models.

125 The view that some responses may occur only under specific conditions of exposure or are dependent on ill-defined biological factors makes broad generalisations difficult, if not impossible, to draw. There have been suggestions that the time-weighted, average field strength, used in many studies as a measure of exposure, is not truly representative of the 'effective' exposure metric. Some studies have suggested the existence of frequency and amplitude response 'windows', and that modulation frequency, exposure pattern and duration may also influence the experimental outcome. These uncertainties stem from the absence of a plausible biophysical mechanism of interaction on which an appropriate exposure metric could be based.

126 Other uncertainties result from an incomplete understanding of the distribution of sensitivity to EMF effects, particularly of weak induced electric fields, amongst the population. Specific issues are age-related differences and those resulting from medical conditions or treatment. In addition, there remains some uncertainty about possible effects on circadian and other biological rhythms and the implication any effect might have for human health – further study is required. Finally, there is the acknowledged uncertainty of extrapolating results to humans from data obtained using various animal species and *in vitro* experimental models.

Summary

127 With regard to effects of surface charge induced by exposure to low frequency electric fields, exposure to fields less than 5 kV m^{-1} will have a low risk of painful discharge from a person to ground. Thresholds for the discharge from an object through a grounded person depend on the size of the object and therefore require specific assessment. In environments where appropriate control is possible, the risk of painful discharge can be minimised by engineering or administrative controls (including training).

128 The primary means by which electric fields and currents induced in the body by exposure to external fields interact with biological tissue is through voltage-gated ion channels situated in cell membranes. The effect is to alter the flux of certain ions, and the electric potential difference, across the cell membrane leading to subsequent biological responses. The most sensitive tissues are those comprising interacting networks of electrically excitable tissue, such as the central, autonomic and enteric nervous systems. Thresholds of between about 100 and 1000 mV m^{-1} have been determined in CNS tissue *in vitro*. The neural circuitry of the retina is taken as a good model for induced electric field effects on central nervous system neuronal circuitry in general. Thresholds of around 10–60 mV m^{-1} in the extracellular fluid of the retina have been calculated for the phosphene response of volunteers, but there is considerable uncertainty associated with these values, and their extrapolation to values appropriate for the whole tissue, as used by dosimetric models, is complex. These uncertainties can only be resolved through further experimental and dosimetric investigation. The threshold for effects in central, autonomic and enteric nervous system tissue is taken to be 100 mV m^{-1}, possibly as low as 10 mV m^{-1}. This spans the range of values identified by the ad hoc expert group on weak electric fields (Appendix A) for normal and particularly sensitive individuals. The heart, other muscle tissue and 'non-excitable' tissues with voltage-sensitive ion channels are expected to show a lower sensitivity.

129 Sensitivity to electric fields induced within the body will vary within the population. People who are particularly sensitive will include those with epilepsy, a family history of seizure, or those using tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold. The developing nervous system *in utero*, and in neonates and young children, may also be considered more sensitive.

130 The frequency response of these effects is unknown. Ion channel kinetics suggest that the thresholds may be constant over the frequency range 10 Hz – 1 kHz and would apply to a minimum of 1000 interacting cells, which would occupy approximately 1 mm^3 in CNS tissue.

131 In addition, a number of studies suggest that low frequency EMFs, particularly magnetic fields in excess of about 100 μT, may induce a variety of subtle responses in biological systems, as well as those attributable to the effects of either surface charge or the induced electric field. However, the pattern of reported responses is diffuse and inconsistent. Furthermore, many tend to be small in magnitude and often fail to be replicated. Overall, none is considered sufficient to provide a coherent framework on which to base restrictions for human exposures.

A critical evaluation has been carried out of biological studies relevant to the assessment of possible adverse health effects of exposure to low frequency electric and magnetic fields. With regard to electric fields and currents induced in the body by these external fields, the most plausible and coherent set of data from which guidance can be developed concerns weak electric field interactions in the CNS and other excitable tissues. In addition, these data show 'dose–response' relationships. A cautious approach has been used to derive thresholds for adverse health effects.

Other studies reviewed lack plausibility, coherence and consistency precluding a positive role in this process.

Thresholds for adverse health effects of the electric fields and currents induced in the body by exposure to low frequency electric and magnetic fields on the central, autonomic and enteric nervous systems are judged to be at induced electric field strengths in the extracellular fluid of around 100 mV m^{-1} and possibly as low as 10 mV m^{-1}. However, there is considerable uncertainty associated with these values. The frequency response of these effects is not, at present, clear. Ion channel kinetics suggest that they may occur over the frequency range 10 Hz – 1 kHz and in a minimum of 1000 interacting cells, which would occupy approximately 1 mm^3 in tissue of the CNS.

People with epilepsy, a family history of seizure, or those using tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold are likely be more sensitive to weak electric field effects than people without these conditions. The developing nervous system *in utero*, and in neonates and young children is also considered more sensitive.

With regard to the effects of surface electric charge, exposure to a power frequency electric field of less than 5 kV m^{-1} should not result in painful discharge from a person to ground. Thresholds for the discharge from an object through a grounded person depend on the size of the object and therefore require specific assessment. Exposure to electric fields of less than 15 kV m^{-1} should not result in unpleasant direct perception effects in people.

DOSIMETRY

132 Computational dosimetry provides a link between external non-perturbed EMFs and the fields induced within the body. This gives guidance on the choice of reference levels in relation to basic restrictions.

133 Exposure guidelines provide basic restrictions on induced current density to prevent effects on CNS functions for frequencies up to 10 MHz.

134 The state-of-the-art approach to deriving reference levels is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic models of the body. Subsequent sections describe the calculations of induced electric fields and current densities from low frequency magnetic and electric fields.

Induced current densities from low frequency magnetic fields

Computational methods

135 The first method applied to anatomically complex voxel models of the human body was the impedance method (Gandhi et al, 1984; Orcutt and Gandhi, 1988; Gandhi and Chen, 1992; Xi et al, 1994). The target body is split into cuboid cells or voxels, which are then further, differentiated into a three-dimensional network of impedances. The

time-varying magnetic field impresses a voltage around the closed loop of each face. A system of coupled equations for the loop currents on the orthogonal faces of the cells results and can be solved iteratively. The electric fields along the edges of the cuboid cell are then obtained to produce an average value in the cell and thence a value for the current density. More recently the Scalar Potential Finite Difference (SPFD) method has been introduced (Dawson et al, 1996; Dawson and Stuchly, 1997). This method incorporates the applied magnetic field source as a vector potential term in the electric field. This equation for the electric field is then transformed into a scalar potential form, which is then solved using finite-differences. This continuous equation can be mapped on to a three-dimensional domain of cells. The finite-difference technique can then be used to define the potential at nodes where the cells meet in terms of potentials at neighbouring nodes and the conductivities of neighbouring cells evaluated at half-node points, ie on the edges half-way between nodes, along with vector potential values at these half-nodes. The equation for the potential can then be solved iteratively or by matrix methods. A feature of both methods is that the computational space is confined to only the voxels of the body. A recent review of numerical methods and interaction mechanisms can be found in Stuchly and Dawson (2000).

Calculations of induced fields

136 Dimbylow (1998) calculated current density in the fine resolution (2 mm) NORMAN phantom (see Chapter 2, paragraph 34) for uniform magnetic fields alligned with the front, side and top of the body for frequencies from 50 Hz to 10 MHz. Both the impedance and SPFD methods were used to provide mutual corroboration. At 50 Hz they agreed to within 2% for AP (front-to-back), 3% for LAT (side-to-side) and 1% for TOP (top-to-bottom) orientation. The scalar potential method requires less computational memory and is much quicker than the impedance method so this was chosen to perform the full range of calculations up to 10 MHz. The outer layer of the eye in NORMAN was not initially differentiated from the humour. The retina is important because of the induction of phosphenes. Therefore, because the humour and sclera have quite different conductivities the outer layer of the eye was reclassified as sclera. The rear part of this shell was then considered to be the retina for the analysis of induced current density. Results are presented for the current density averaged over 1 cm^2 in muscle, heart, brain and retina.

137 Dawson and Stuchly (1998) have calculated induced electric fields and current densities in the modified Yale phantom (see Chapter 2, paragraph 36) at a resolution of 3.6 mm. The results are given for various organs in terms of average and maximum values for 60 Hz uniform magnetic fields in three orthogonal orientations. The SPFD method with an appropriate matrix conditioner and a conjugate gradient solver were used to model the problem. It is difficult to compare the two sets of calculations because of the differing averaging methods and model resolutions. The NRPB calculations with NORMAN have a 2 mm resolution compared with 3.6 mm for the University of Victoria results, so the maximum values over any voxel will tend to be greater. Hence for the whole body the maximum from the NORMAN calculations is 82.2 A m^{-2} per tesla at 50 Hz for AP orientation compared with 63.7 A m^{-2} for the UVic results converted to 50 Hz. The corresponding values for the maximum electric field are 381 against 307 V m^{-1}. The averages performed in NORMAN are over 1 cm^2, whereas UVic

gives maximum and average values in an organ so the NORMAN values should be intermediate. Converting the UVic data to an applied 1 T field at 50 Hz gives maximum and average values in the brain of 6.07 and 0.746 A m^{-2} for AP orientation. The corresponding electric field values are 60.7 and 8.83 V m^{-1}. The maximum current density from Dimbylow (1998) in the brain averaged over 1 cm^2 is 3.59 A m^{-2} and the electric field is 44.9 V m^{-1} (using a conductivity, $\sigma = 0.08$ S m^{-1}). It can be seen that despite different resolutions and averaging metrics the two sets of calculations are consistent. Differences in current density distribution can be attributed to the difference in model shape especially for the orientation from side to side. The UVic model has hands clasped in front and in contact with the rest of the body, thus forming longer current loops in some body regions. In contrast, NORMAN has the arms at the side and not in contact with the rest of the body.

138 Stuchly and Gandhi (2000) performed a comparison of induced fields for exposure to 60 Hz applied electric and magnetic fields. The University of Utah group (see Chapter 2, paragraph 35) used the impedance method on the 6 mm resolution version of their phantom and the University of Victoria group used the SPFD method on the 3.6 and 7.2 mm versions of their model. The average induced electric field in the brain for a 50 Hz, 1 T field for AP orientation was 9.58 V m^{-1} for the Utah model, and 8.83 and 9.58 V m^{-1} for the 3.6 mm and 7.2 mm Victoria models. The average over 1 cm^2 from the NRPB calculations (Dimbylow, 1998) was 44.9 V m^{-1}. The corresponding average induced current density in the brain was 1.95 A m^{-2} for the Utah model and 1.15 A m^{-2} for the 7.2 mm Victoria model. The average over 1 cm^2 from the NRPB calculations was 3.59 A m^{-2}. Stuchly and Gandhi concluded that the obtained differences for the dosimetric data of human models exposed to electric and magnetic fields could be rationally explained (see paragraph 151).

139 Later work by Gandhi et al (2001a) calculated current density averages over 1 cm^2. They used the impedance method on the 6 mm version of their model but the region around the spinal cord was expanded to the original dimensions, 1.974 × 1.974 × 3.0 mm. The current densities were averaged over 1 cm^2 by interpolation from the 6 mm grid. They obtained values of 2.25 A m^{-2} for the brain/spinal cord and 7.76 A m^{-2} for the heart for an AP orientation, 50 Hz, 1 T field compared with 3.59 and 5.26 A m^{-2}, respectively, from the NRPB calculations. The Gandhi et al brain/spinal cord values are 37% lower than those from NORMAN. This may be due to the coarser resolution calculations and problems with interpolation on to a 1 cm^2 surface. The heart results are higher because the Utah phantom uses a composite heart muscle/blood tissue rather than discrete heart muscle and blood as in NORMAN.

140 Gandhi and Kang (2001) have also calculated current densities from non-uniform fields from electronic surveillance devices. They scaled the Utah adult model to represent 10- and 5-year old children. They found that, for the representative devices and particular operating conditions chosen, the current density averaged over 1 cm^2 in the brain/spinal cord was lower than the ICNIRP restrictions for the taller model of the adult, but may approach or even exceed them for the shorter models of the 10- and 5-year-old children. This is a geometric effect due to the brain for the shorter models being in considerably higher non-uniform fields from the particular device than the brain of the taller adult. Other example of application to non-uniform fields can be found

in Dawson et al (1999) where realistic postures and configurations of three-phase current carrying conductors are considered.

Induced current densities from low frequency electric fields

Computational methods

141 The difficulty in calculating the interaction of low frequency electric fields with the body, as opposed to magnetic fields, is that the body perturbs the applied field and this perturbation must be accommodated in the specification of the boundary conditions. The Finite-Difference Time-Domain (FDTD) method (Taflove, 1995) is not usually applied at low frequencies because the time step is related to the resolution of the model which means that the number of steps required to reach equilibrium is proportional to the inverse of the frequency. Furse and Gandhi (1998) applied the FDTD method on a 6 mm resolution grounded MRI based model. The FDTD scheme was run at 10 MHz, but using the conductivities appropriate to 60 Hz. The calculated induced current densities were then linearly scaled with frequency to obtain the values at 60 Hz.

142 Dawson et al (1998) used a hybrid two-stage approach. A low resolution (7.2 mm) solution was performed by a quasistatic-FDTD algorithm (De Moerloose et al, 1997). In this steady state quasistatic approximation of FDTD the fields exterior to conductors all have the same phase as the incident field. Interior fields are of first order and are proportional to the time derivative of the incident field. If a ramp function is used for the incident field, all fields will eventually have a linear (exterior) or constant (interior) behaviour. The resulting surface charge density was extracted from the potentials and interpolated on to the body surface of the higher resolution model (3.6 mm) to provide the source term for internal calculations using a scalar potential method (Dawson et al, 1996).

143 Dimbylow (2000), using NORMAN, solved a potential equation on a series of nested subgrids decreasing from 32 mm to 2 mm. The outer region of the domain extended sufficiently so that the perturbation in the applied field, due to the phantom, was small at the periphery whilst the grid near and in the phantom was small enough to model the structural details. The solution of the potential equation is divided into two parts. First, the coupling between the externally applied electric field and the human body, which is deemed to be a conductor at low frequencies, is calculated to provide the surface charge. This charge is then used as a boundary condition to calculate the internal potential and hence induced fields and current densities in the body at a resolution of 2 mm.

Calculations of induced fields

144 Current density distributions in a fine resolution (2 mm), anatomically realistic voxel model of the human body have been calculated (Dimbylow, 2000) for uniform, low frequency vertically aligned electric fields for grounded and isolated conditions from 50 Hz to 10 MHz. Hybrid FDTD methods were used as well as the nested finite-difference potential method to provide mutual corroboration. The calculated short-circuit current for the grounded case at 50 Hz using the potential formulation is 14.8 μA per kV m^{-1} compared with 14.0 μA (a difference of –5%) for the FDTD method and 14.7 μA (linearly scaled from 17.6 μA at 60 Hz) obtained by Dawson et al (1998) for a 1.77 m, 76 kg phantom and around 14.3 μA, similarly scaled from the work by Furse and

Gandhi (1998) for a 1.764 m, 71 kg phantom. The FDTD calculations of current density are within 2% of those from the potential method for the maximum value in any 2 mm voxel, for both the grounded and isolated cases, and within 9% and 2% for the averages over 1 cm^2 in the retina for the grounded and isolated cases.

145 Furse and Gandhi (1998) calculated electric fields and currents induced in the 6 mm version of the Utah model. FDTD calculations were performed at 10 MHz and were scaled using a quasistatic approximation to 60 Hz. Converting their results to an applied field of 1 $V m^{-1}$ at 50 Hz yields minimum, average and maximum values of current density in the brain of 0.059, 0.157 and 0.694 $\mu A m^{-2}$. The Dimbylow (2000) value averaged over 1 cm^2 in brain/spinal cord is 0.176 $\mu A m^{-2}$ and the maximum value is 0.413 $\mu A m^{-2}$.

146 Stuchly and Gandhi (2000) performed a comparison of induced fields for exposure to 60 Hz applied electric and magnetic fields. The University of Utah group (Furse and Gandhi, 1998) used the FDTD method scaled in frequency on the 6 mm resolution version of their phantom and the University of Victoria group (UVic) used the hybrid quasistatic FDTD/SPFD method (Dawson et al, 1997) on the 3.6 and 7.2 mm versions of their model. The average induced electric field in the brain in a grounded phantom for a 50 Hz, 1 $V m^{-1}$ field was 0.892 $\mu V m^{-1}$ for the Utah model (6 mm resolution, $\sigma_{brain} = 0.17 S m^{-1}$), and 0.617 $\mu V m^{-1}$ for the University of Victoria model (7.2 mm resolution, $\sigma_{brain} = 0.1 S m^{-1}$). This compares with the average over 1 cm^2 for the NRPB model of 2.2 $\mu V m^{-1}$ (2 mm resolution, $\sigma_{brain} = 0.08 S m^{-1}$).

147 Hirata et al (2001) calculated induced electric fields and current densities in a rescaled adult model to represent a 5-year-old child and these are compared with those in the full-scale adult, UVic phantom. The calculations were performed with the hybrid approach (Dawson et al, 1998) and a final resolution of 3.6 mm inside the phantom. All three dosimetric organ measures (average, 99th percentile and maximum) of the induced electric field are consistently lower in the organs and tissues of the child's head than in the adult's head. The differences are around 20% and reflect the average field reduction in the head to 67% of the adult. However, this is not necessarily the case for the rest of the body, eg the field values in the heart are higher in the child than in the adult. In conclusion, the volume of the child head and brain is proportionately greater as a fraction of the total body volume than in adults. This results in a lower average current density and electric field in the child's head.

Dosimetric uncertainties

148 Sources of uncertainty in EMF calculations include the reliability of numerical methods, different individual anatomies and postures, resolution and variation in dielectric parameters.

149 Caputa et al (2002) have looked at the reliability of numerical methods and the effects of variations in voxel phantoms on power frequency magnetic field dosimetry. The groups at the University of Victoria and NRPB have calculated the induced electric fields in both the UVic and NORMAN models using independently developed codes. A detailed evaluation has been performed for a uniform magnetic field at 60 Hz. Comparisons of the average (E_{avg}), maximum (E_{max}) and 99th percentile (E_{99}) electric fields for all the organs in the models show differences of 1% or less for the great majority of tissues. Only in a few cases the difference reaches 2%. The influence of the

body model size and shape including anatomy were investigated by comparing the original NORMAN model at 2 mm resolution, a rescaled NORMAN at 4 mm, the original UVic model at 3.6 mm, an expanded UVic model at 1.8 mm, and a 2 mm version of the Brooks digital anatomical man model. The effect of the size is best illustrated by the digital anatomical model which has a mass 42% greater than the reference 73 kg of NORMAN. Correspondingly, the whole-body average electric fields are 44% greater. This is not unreasonable, since the difference in height of the models is small (0.2%), thus the increase in volume (mass) is mainly in the horizontal frontal dimensions of the torso. The actual anatomy of people represented by the models, as well as the accuracy of the models, both influence differences in dosimetric measures. Relatively small organs (such as the testes) or thin organs (such as the spinal cord) indicate large differences in induced electric field strength that can be directly ascribed to the differences in the shape and size of these organs in the models. Differences in current density distribution can be attributed to the difference in model shape especially for the orientation from side to side. The UVic model has hands clasped in front and in contact with the rest of the body, thus forming longer current loops in some body regions. To the contrary, NORMAN has the arms at the side and not in contact with the rest of the body. Regarding the model resolution, the differences for E_{avg} and E_{99} are relatively small. The most apparent and consistent factor is the influence of the model resolution on voxel maximum values. The large values of E_{max} for the high resolution models are inherent in their division into voxels, namely the large current density in the vicinity of the inner corner of a given organ/tissue boundary layer (Dawson, et al, 2001).

150 A limited set of calculations has been performed at NRPB to investigate the effect of variations in dielectric parameters. Firstly, applied low frequency magnetic fields were considered. Here the robust dose quantity is the induced electric field. If all the conductivities of the body are multiplied by a constant factor, say 2.0, then the induced electric field will stay the same as before but the induced current density will increase by a factor of 2.0. The conductivity of the brain alone was changed by factors of 2.0 and 0.5 compared with the Gabriel (1995) value (0.08 S m^{-1}). This resulted in changes of –23% and +30% in the induced electric field, averaged over 1 cm^2, and changes of +54% and –35% in the induced current density. For applied low frequency electric fields the converse is true and the induced current density is the more robust quantity. If all the conductivities of the body are multiplied by a constant factor, say 2.0, then the induced current density will stay the same as before but the induced electric field will decrease by a factor of 2.0. When the conductivity of the brain alone was changed by factors of 2.0 and 0.5 this resulted in changes of +11% and –13% in the induced current density and changes of –44% and +73% in the induced electric field.

151 Stuchly and Gandhi (2000) concluded that the differences for the dosimetric data of human models exposed to low frequency electric and magnetic fields could be rationally explained. Factors are the accuracy of the numerical method, voxel resolution, human body model size and posture, organ size and shape, and dielectric properties. Errors due to numerical methods for average values are around 1–3%. Larger errors are associated with maximum values. Smaller errors in average values and larger maximum values are associated with decreasing voxel size, especially for small organs. Body posture has a relatively large effect. For applied magnetic fields the induced electric fields are relatively impervious to the magnitude of the conductivity

but it has a strong effect on the induced current density. On the basis of the comparison presented, it is estimated that the average induced electric field and current density in human organs are known within a factor of two for exposures of the average man to uniform electric and magnetic fields at 60 Hz.

Summary

152 Computational dosimetry provides a link between external non-perturbed EMFs and the fields induced within the body. This gives guidance on the choice of reference levels in relation to basic restrictions. The usual approach to deriving reference levels is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic models of the body.

153 The computational methods for applied magnetic fields most suitable to voxel models are the impedance method and the scalar potential finite-difference (SPFD) method. A feature of both methods is that the computational space is confined to the voxels of the body. The difficulty in calculating the interaction of low frequency electric fields with the body, as opposed to magnetic fields, is that the body perturbs the applied field and this perturbation must be accommodated in the specification of the boundary conditions. This problem has been approached by modified frequency scaled FDTD methods, hybrid FDTD/quasistatic potential calculations and nested grid potential calculations. A recent review of numerical methods and interaction mechanisms can be found in Stuchly and Dawson (2000).

154 Induced internal electric fields and current densities have been calculated in a number of voxel models for applied uniform power frequency magnetic fields and for electric fields. It is important to consider children in the analysis of non-uniform fields, eg the magnetic fields from electronic surveillance devices, because the brain may be in a higher non-uniform field from the particular device than the brain of the taller adult.

155 Stuchly and Gandhi (2000) concluded that the differences for the dosimetric data of human models exposed to low frequency electric and magnetic fields could be rationally explained. Factors are the accuracy of the numerical method, voxel resolution, human body model size and posture, organ size and shape, and dielectric properties. On the basis of the comparison presented, it is estimated that the average induced electric field and current density in human organs are known within a factor of two for exposures of the average man to uniform electric and magnetic fields at 60 Hz.

The usual approach to deriving reference levels is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic voxel models of the body.

The differences for the dosimetric data of human models exposed to low frequency electric and magnetic fields can be explained in terms of the accuracy of the numerical method, voxel resolution, human body model size and posture, organ size and shape, and dielectric properties. It is estimated that the average induced electric field and current density in human organs are known within a factor of two for exposures of the average man to uniform electric and magnetic fields at power frequencies.

It is important to additionally consider children when calculating current densities from low frequency magnetic devices when the field is non-uniform.

5 Electromagnetic Fields of Frequencies Above 100 kHz

1 In this chapter, scientific data relevant to the development of exposure guidelines for time-varying electromagnetic fields (EMFs) of frequencies greater than about 100 kHz are addressed. These fields have frequencies in the radiofrequency (RF) range where the dominant identified and well-understood interaction processes and adverse health effects are due to the heating of body tissues from induced internal electric fields and currents. However, other adverse health effects due to electrostimulation of body tissues are also possible at frequencies up to about 10 MHz and these are considered in Chapter 4. The reviews summarised in this chapter cover a wide range of possible biological effects and disease outcomes. Thus this chapter constitutes a comprehensive summary of relevant published epidemiological and biological studies and computational dosimetry.

EPIDEMIOLOGY

2 A number of studies have examined the health of people exposed to RF EMFs, through the use of mobile phones, work, hobbies, or residence near radio or television transmitters. These studies have been reviewed by a European Commission expert group (McKinlay et al, 1996; Veyret et al, 1999), French expert groups (Zmirou, 2001; Aran et al, 2003), the French Senate (Lorrain and Raoul, 2002), the Independent Expert Group on Mobile Phones (IEGMP, 2000), the Royal Society of Canada (Krewski et al, 2001a,b), the Advisory Group on Non-ionising Radiation (AGNIR, 2001c, 2003), Boice and McLaughlin (2002), and the Swedish Radiation Protection Authority (SSI, 2003). Many of these studies have looked at cancer risks, but other endpoints such as pregnancy outcome have also been considered.

3 Findings from these studies – which have focused on the possible non-thermal health effects of RF EMF exposure – are reviewed below. Studies of the effects of heat on mortality and morbidity are also reviewed, and the relevance of these studies to thermal health effects of RF EMF exposure is considered.

Cancer

4 A review by Elwood (1999) concluded that the epidemiological evidence linking RF EMF exposures and cancer was weak in regard to its inconsistency, the design of the studies undertaken as of that time, the lack of detail on actual exposures, and the limitations of the studies in their ability to deal with other likely relevant factors. In addition, there may have been biases in some studies. In its review of occupational studies and studies near broadcasting facilities, IEGMP (2000) concluded that the overall balance of evidence did not indicate that RF radiation affected the risk of cancer in people. However, many of the occupational studies had low statistical power, some had methodological defects, including little or no exposure assessment, and the types of

exposure investigated varied between studies. Furthermore, the studies near radio and television transmitters had major limitations, including the lack of measured field levels in the analyses. In addition, at the time of the IEGMP report, there had been few studies of mobile phones and cancer. Thus, whilst the epidemiological studies conducted up to the early part of 2000 did not give cause for concern, IEGMP concluded that this research had too many limitations to give reassurance that there was no hazard.

5 Since early 2000, further studies have been published of cancer in relation to the use of mobile phones. AGNIR (2001c) reviewed two case–control studies of brain tumours in the USA (Muscat et al, 2000; Inskip et al, 2001) and a cohort study in Denmark (Johansen et al, 2001). The first two of these studies were hospital based, and information on mobile phone use was collected through interviews with the study subjects. In contrast, the Danish study used information from operating companies on mobile phone use, and so the assessment of exposure was likely to be less precise than in the American studies. However, whereas the Danish study used a national population registry as the basis of its cohort, the use of hospital controls in the American studies might have raised the potential for selection bias. A subsequent case–control study in Finland found that mobile phone use was not associated with brain tumours or salivary gland cancers overall, but there was a weak significant association between gliomas and the use of analogue mobile phones; however, this study lacked information on individual exposures (Auvinen et al, 2002). The case–control studies in the USA did not find associations between mobile phone use and the risk of acoustic neuroma (Inskip et al, 2001; Muscat et al, 2002), but the small numbers of cases both here and in another American study (Warren et al, 2003) limited inferences.

6 The preceding studies were generally based on several hundred people with a brain tumour, plus controls, and had limited opportunity to investigate any effects that might arise 10 or more years after exposure. In contrast, a recent study in Sweden analysed data on about 1300 people with a brain tumour and the same number of controls, of whom several tens had used mobile phones more than 10 years previously (Hardell et al, 2002). A subsequent paper based on the same study, but with a different method of analysis, gave similar results (Hardell et al, 2003). A raised brain tumour risk was found in the Swedish study among mobile phone users, particularly those who reported using an analogue phone at least 5–10 years previously. There were also indications of a similar increase in risk among users of cordless phones based on a long latency. Furthermore, the risk among analogue mobile phone users – which in relative terms was greatest for acoustic neuroma – was not raised to a statistically significant extent after taking account of the fact that some people had used more than one type of phone. Since RF exposures from cordless phones are much lower than those from analogue mobile phones, the raised risks reported in the Swedish study may be due – at least in part – to biased recall of phone use 5–10 or more years previously. Such a bias might also explain why there tended to be a raised risk for tumours in the side of the head nearest to where the phone was reported to have been used, but a decreased risk for tumours in the opposite side of the head.

7 Recent studies of cancer and occupational exposures to RF fields (eg Baumgardt-Elms et al, 2002; Groves et al, 2002; Kliukliene et al, 2003) have given variable results. Like earlier studies that have been reviewed, for example, by IEGMP (2000), some of

these studies had methodological problems and the method of exposure assessment varied between them. A report of a raised risk of malignant melanoma of the eye in relation to the use of RF transmitting devices in Germany (Stang et al, 2001) has been criticised for the lack of adjustment for possible confounding factors such as exposure to ultraviolet radiation (Inskip et al, 2001); also, the findings were not supported by a correlation study in Denmark (Johansen et al, 2002) or by temporal trends in disease incidence in the USA (Inskip et al, 2003).

8 An analysis reported a statistically significantly raised risk of childhood leukaemia with proximity to a high power radio station in Rome, with less evidence for an increase in adult leukaemia (Michelozzi et al, 2002). However, these findings were based on small numbers of cases. They also differ from results around radio and television transmitters in Great Britain, where there was some evidence of an increased risk with increasing proximity for the incidence of adult leukaemia but not childhood leukaemia (Dolk et al, 1997). Furthermore, studies around transmitters such as these are limited by a lack of exposure data. Such problems were more severe in a recent correlation analysis of melanoma of the skin and frequency modulation broadcasting in Nordic countries (Hallberg and Johansson, 2002).

9 In its recent review, AGNIR (2003) concluded that while there have been positive findings in some studies for risks of specific cancers in relation to mobile phone use or to occupational or residential RF field exposure (or potential for exposure), no relataion has been shown consistently. There has also not been a convicing demonstration of a dose–response or duration–response relationship. However, AGNIR noted that the design of the studies has often been deficient. Hence, although the studies do not suggest a raised risk of cancer, they do not rule one out, especially in relation to large cumulative exposures to mobile phones and possible effects occurring many years after their use.

Other health outcomes

10 Several cohort studies of occupational groups exposed to RF EMFs have examined non-cancer mortality and, in some instances, morbidity. IEGMP (2000) concluded that these studies did not provide any overall evidence of a hazard. Furthermore, case–control studies of pregnancy in physiotherapists have not, overall, supported a relation of microwave exposure with spontaneous abortion or other adverse outcomes (IEGMP, 2000; Krewski et al, 2001a). However, IEGMP concluded that this research had too many limitations to give reassurance that there was no hazard. It also reviewed reports of symptoms such as fatigue, headache and feelings of warmth behind the ear occurring during or shortly after the use of mobile phones, and found it unclear as to what extent, if any, these symptoms were caused by RF radiation (IEGMP, 2000). AGNIR (2003) reached similar conclusions.

Effects of heat on mortality and morbidity

11 Various studies of temporal changes in population mortality rates have shown associations with temperature (eg Keatinge et al, 2000; Curriero et al, 2002). In particular, episodes of very hot or very cold temperatures are associated with increased mortality, mainly from cardiovascular disease. Furthermore, it has been suggested that a sudden and unexpected change of as little as 2°C in external temperature, giving no time for

adaptive changes, could lead to an extra 1900 heat-related deaths per year in Britain (Donaldson et al, 2003). However, it should be stressed that these studies of mortality and temperature have been conducted at a population level, and that individual data have often been lacking on other factors associated with particularly hot or cold periods that affect mortality rates, eg the prevalence of influenza or air pollution. In addition, environmental temperature, humidity and physical exertion would also modify cardiovascular responses to additional heat loads. Consequently, it is difficult to use these population studies of external temperature changes to quantify the mortality that might be produced by an additional heat load due to RF exposures, although the possibility of an effect cannot be excluded, particularly in periods of hot weather. This topic is considered further in paragraphs 23–39.

12 A number of studies have indicated adverse effects on human prenatal development – particularly on the central nervous system – from maternal hyperthermia (Graham et al, 1998). However, it has often been difficult to separate any influence of heat alone from maternal metabolic changes occurring in fevers (Edwards et al, 2003). A few prospective studies have considered groups exposed to both sources of hyperthermia. For example, Milunsky et al (1992) reported a raised risk of neural tube defects in relation to use of a hot tub or sauna, or to a report of fever, in the first trimester of pregnancy. Although this study was based on a large cohort and used information on individual exposures collected during pregnancy, the small numbers of cases limit inferences. Furthermore, when considering RF EMF induced heating, it should be noted that any adverse effect would be modified by environmental temperature and physical exertion. Consequently, it is difficult to use the studies of maternal hyperthermia to quantify teratogenic effects that might be produced by internal heating due to RF exposures. Similarly, overheating has been associated with sudden infant death syndrome (eg Fleming et al, 1990).

Epidemiological uncertainties

13 Many of the epidemiological studies of the potential effects of RF exposure conducted up to the late 1990s had included either poor measures of exposure or none at all (Swerdlow, 1999). For example, some studies have used current job title or distance of place of residence from an RF transmitter as a proxy for exposure. However, exposures are likely to be heterogeneous between workers with the same job title, and exposures from transmitters are unlikely to be determined solely by proximity. Some, although not all, of the recent studies of mobile phone users have been able to collect more specific information relevant to exposures – for example, by asking the study subjects about their use of mobile phones (Muscat et al, 2000; Inskip et al, 2001). These studies have included several hundred people with a brain tumour, and therefore had reasonable statistical power to detect an overall association, although this would have been reduced by misclassification of exposures. However, the power to address more detailed issues such as the use of digital as opposed to analogue mobile phones and risks for specific types of brain tumours has been limited. In addition, given that these phones have only been used widely in recent years, epidemiological studies of users provide little information on whether there may be health risks many years after initial exposure. Another potential difficulty in retrospective studies is the possibility of recall

bias, ie whether the subject's ability to recall past exposures differs between those who developed the disease under study and those who did not.

14 In contrast to the cohort and case–control approach used for some of the studies of RF exposures (particularly of mobile phone users), studies of the health effects of environmental temperature changes have been based largely on aggregated data. Consequently, it has not been possible in general to take account of factors at the individual level that may have influenced the risks of mortality or morbidity. Studies of prenatal development following maternal hyperthermia have generally used individual-level data, but it was difficult in many of these studies to separate any effects of heat *per se* from those associated with other sources of hyperthermia. The estimation of risks from RF EMF induced heating is complicated further by the modification of such effects by environmental temperature and physical exertion.

Epidemiological studies of groups exposed to RF EMFs have been variable in quality. Some studies have been limited by low statistical power or a lack of exposure measurements, while others may have been affected by bias.

The overall evidence from the more methodologically sound studies, including those conducted recently of mobile phone users, does not indicate that RF exposures increase the risk of cancer. However, the evidence is not conclusive. In particular, these studies have generally provided little information on whether risks might be raised many years after exposure, or on some specific types of exposure, eg from the use of digital mobile phones. One recent large study reported a raised risk of brain tumours some years after using an analogue mobile phone, but this finding may be due – at least in part – to bias in the recall of phone use.

Studies of occupational RF exposures do not indicate raised risks of non-cancer mortality or adverse pregnancy outcome, although again it is not possible to exclude the possibility of a small risk.

Mortality, mainly from cardiovascular disease, has been shown to be raised in populations exposed to high or low temperatures, and there are indications that maternal hyperthermia may lead to central nervous systems defects in offspring. However, for several methodological reasons, it is difficult to use these studies to quantify effects on mortality and prenatal development associated with internal heating from RF exposures.

BIOLOGY

15 The biological effects of RF EMFs have continued to be studied using a wide range of frequencies, modulations and experimental models. Earlier studies tended to investigate frequencies set aside for industrial, scientific and medical use (ISM frequencies) and to a lesser extent those used in radar and communications. More recently, the growth and development in personal mobile communications has focused attention on the frequencies associated with this technology. Heating continues to be the major effect of exposure to RF EMFs. However, concern has been expressed that exposure at levels too low to cause significant heating may nevertheless cause detrimental effects and, in particular, increase the risk of cancer.

16 This section presents a summary of the biological effects of RF EMFs with frequencies from 100 kHz to 300 GHz. These studies have been much examined and assessed. Notable reviews include those by NCRP (1986), WHO (1993), and an EC expert group (McKinlay et al, 1996; Veyret et al, 1999). Many other reviews and critiques of this literature have been published, including those by ICNIRP (1996), the Health Council of the Netherlands (HCN, 1997, 2000, 2002), AGNIR (2001c), and the Swedish Radiation Protection Authority (SSI, 2003). Of particular importance are the comprehensive reviews by IEGMP (2000), Zmirou (2001), the Royal Society of Canada (Krewski et al, 2001a,b), and AGNIR (2003).

17 The consensus remains that the majority of reported effects result from either rises in tissue or body temperature of about 1°C or more, or in physiological and behavioural responses for minimising the total heat load (Saunders et al, 1997). However, comparatively few studies have attempted to define more rigorously the basis of previous guidance (eg NRPB, 1993) – namely whole-body and localised heating. There is, however, an established literature on the physiological effects of heat, and on the consequences of local temperature rises, summarised recently at a WHO workshop (WHO, 2003b), from which information relevant to the development of guidance can be derived. This workshop addressed the effects of heat seen in healthy people and in those vulnerable to heat stress. Similar conclusions were derived, mostly for healthy people, by Adair and Black (2003).

18 In addition, some studies have reported biological effects in the apparent absence of overt heating. While the possibility of non-thermal effects cannot be completely dismissed, none is considered sufficiently well defined to be used as a basis for guidance. The possible effects of exposure to RF EMFs at non-thermal levels are also considered in this chapter.

Whole-body heating

19 RF energy absorbed by the body results in heat due to an increase in molecular rotational and translational kinetic energy. The absorbed heat energy is distributed throughout the body by the circulation of blood and is eventually lost to the external environment. Significant whole-body heating has a major impact on cardiovascular physiology and thermoregulatory ability. In addition, the ability to carry out cognitive tasks is also likely to be compromised before physiological limits of tolerance are reached.

20 Cardiovascular responses to heat and exercise are central to body temperature regulation in humans. Except in various pathological conditions and during heavy exercise, the 'core' body temperature is maintained under a wide range of environmental conditions at a value of about 37°C with a circadian fluctuation of about ±0.5°C. Heat gained at rest, during exercise or exposure to RF EMFs, has to be compensated by heat loss and is often accompanied by a small increase in heat storage (Gordon, 1984).

21 Values for whole-body metabolic heat production can vary in the average population from about 1 W kg^{-1} at rest to about 10 W kg^{-1} during heavy exercise, but may be much higher during sports activities, for example. Typical values for metabolic heat production for many industrial jobs have been estimated to vary from about 2.5 W kg^{-1} for light manual work to 6 W kg^{-1} for heavy manual work (NIOSH, 1980). The

principal heat loss mechanisms in humans are radiant and convective heat loss from the skin through increased skin blood flow and evaporative heat loss from sweat. Heat storage reflects shifts in both peripheral and core temperatures and occurs, for example, during heavy exercise or in hot, humid environments. Prolonged rates of increase in heat storage, such as 0.5–1.0 W kg^{-1} for 1–2 hours, will lead to unacceptable rises in body temperature (Gordon, 1984). In moderate conditions, however, increased skin blood flow will increase heat storage through an increase in the temperature of the peripheral tissues of the body, increasing heat loss without necessarily increasing core temperature.

22 Humans possess comparatively effective heat loss mechanisms; the principal effectors are the sweat glands and cutaneous blood vessels (Nadel, 1980, 1984, 1985; Rowell, 1983; Jessen, 1987). 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 animal species. Skin blood flow can increase from approximately 0.2–0.5 litres per minute in thermally neutral conditions, to values exceeding 7–8 litres per minute during severe hyperthermia. A dense network of capillary loops empties into a capacious sub-papillary venous plexus that constitutes a large potential blood reservoir. Cutaneous venous volume rises with increased blood flow so that, at any given flow rate, flow transit time increases permitting greater heat exchange with the skin. From there, heat is lost to the environment, mainly through convection and, under more severe heat stress, through evaporation of sweat.

Circulatory adjustments to heat stress

23 The principal cardiovascular adjustments to heat stress have been described by Rowell (1983). Supine, resting, healthy volunteers were heated to the limits of their thermal tolerance (core temperature of about 39°C) as cardiac output increased by 6.6 litres per minute. The rise in skin blood flow was found to exceed the rise in cardiac output because blood flow to other major vascular beds was decreased. Mean arterial pressure decreased slightly and then recovered, but central venous pressure decreased markedly.

24 The effectiveness of control of body temperature under heat stress depends on the threshold and the sensitivity (or gain) of the heat dissipation responses. These vary widely between individuals and are subject to many factors (Nadel, 1985) including the time of day, blood volume and the level of physical fitness and acclimation to heat. Sweat rates around 1–1.5 litres per hour are not uncommon, and may reach up to 2 litres per hour in fit individuals providing a potential evaporative rate of heat loss in excess of 1 kW (about 14 W kg^{-1} in a 70 kg human). In the absence of adequate rehydration this deprives the body of fluid from all body compartments, including the vascular component (Nadel, 1980, 1984, 1985). Both exercise and dehydration compromise temperature regulation in hot environments by limiting the blood flow available to the skin. Reflexes that aid in the maintenance of central circulating blood volume and blood pressure take precedence, overriding the thermoregulatory signals for cutaneous vasodilation and so reducing heat loss to the environment. Reduced blood volume also decreases the sweating rate at any given body temperature. A loss of body water of more than 3% of body weight constitutes clinical dehydration and is

associated with early signs of heat-related disorders such as light-headedness and disorientation (Nadel, 1984).

Physiological limits on heat exposure during physical work

25 Consideration of the well-being of healthy workers undertaking manual labour in hot environments has prompted the development of limits on exposure dependent on several physiological criteria such as sweat rate, percentage water loss, heat storage and deep body (core or rectal) temperature. The two main health effects that have usually been considered are dehydration and heat stroke (heat induced decrements in cognitive performance are considered elsewhere). Heat stroke (see below) is the most serious, often fatal consequence of excessive heat exposure and occurs at core temperatures in excess of 40°C (Malchaire et al, 2000). The physiological criteria for limiting work in hot environments in ISO 7933 (ISO, 1989) have recently been reviewed (Malchaire et al, 2000, 2002). These authors focused particularly on work that described the population distribution of rectal temperature in groups of subjects during or after exposure to heat in various working conditions. They concluded that rectal temperatures should be restricted to a maximum of 38°C in order to minimise the risk of heat-related disorder. They also noted that a loss of body water of around 2–3% body weight may lead to heat stress and heat-related illness, and that there is a need for regular rehydration and salt intake, since the thirst sensation is not sufficient to ensure that this would otherwise take place.

Physiological responses in healthy volunteers exposed to RF EMFs

26 The physiological responses of healthy volunteers to RF EMFs have been studied mostly by two groups of researchers. Shellock and colleagues have examined the thermoregulatory consequences of acute abdominal exposure at 64 MHz magnetic fields during clinical magnetic resonance diagnostic procedures, while Adair and co-workers have looked at the consequences of whole- or partial-body acute RF exposure at 450 or 2450 MHz.

27 The acute exposure of volunteers to 64 MHz for 30 minutes at whole-body SARs of 2.7 to 4.0 $W\,kg^{-1}$ or 16 minutes at 6 $W\,kg^{-1}$ resulted in small increases in body temperature (0.1–0.4°C), heart rate, and localised sweating and increased skin blood flow (Shellock et al, 1989, 1994). All of the subjects reported that they felt warm during the procedure and each of them had visible signs of perspiration on their forehead, chest and abdomen. Volunteer exposure to 450 or 2450 MHz for 45 minutes at peak SARs (on the back) of about 6 or 8 $W\,kg^{-1}$ at several different environmental temperatures similarly resulted in vigorous increases in sweating rate on the back and chest (Adair et al, 1998b, 1999, 2001a,b). These effects were directly related to power density, peak SAR and environmental temperature.

28 Overall, these studies indicate that adequately hydrated, passive, healthy volunteers accommodate whole-body RF heat loads of approximately 1 $W\,kg^{-1}$ for 45 minutes at environmental temperatures up to 31°C to 6 $W\,kg^{-1}$ for at least 15 minutes at ambient temperatures with increased skin blood flow and profuse localised sweating but with minimal changes in core temperature. However, whilst increased skin blood flow and profuse localised sweating also ensured small increases in skin temperature in response

to a local peak SAR of about 15 W kg^{-1} at the exposed site, it is not clear how less superficial and less vascular tissues might respond.

Heat-related disorders in adults

29 Heat-related disorders are not uncommon in healthy people unaccustomed to hot environments. Heavy exercise either through work or recreation will further exacerbate any problem, particularly if water and salts lost through sweat are not replenished. In addition, people with a history of heat illness, heat injury or heat intolerance and previous difficulty in acclimatising to the heat are likely to be at increased risk (Kenny, 1985). NIOSH (1986) lists body fat and age as further predictors of heat intolerance but also acknowledges a high degree of individual variation not accounted for by these factors. A number of drugs and chemicals have direct effects on the control of body temperature, or on metabolism or heat production of the body (NIOSH, 1986; BOHS, 1990). Almost any drug that impairs central nervous system activity, cardiovascular reserve or body hydration can reduce heat tolerance (NIOSH, 1986). For example, drugs such as barbiturates or phenothiazines depress reflex regulation of body temperature generally, while anticholinergic drugs specifically suppress sweating and vasodilatation. Alcohol, which interferes with nervous system function and results in dehydration due to the inhibition of anti-diuretic hormone, has been associated with heat stroke (NIOSH, 1986). The potential interactions between such drugs and temperature regulation mechanisms are complex in detail and may depend on a number of factors (BOHS, 1990).

30 A variety of heat disorders have been distinguished clinically when workers have been exposed to excessive heat (NIOSH, 1986). These disorders range from simple postural heat syncope (fainting) to the complexities of heat stroke. A common feature of all heat-related disorders (except for simple postural heat syncope, which is caused by blood pooling in the dilated vessels of the skin and lower body) is some degree of elevated body temperature which may then be complicated by deficits of body water and salt. Even people with access to food and water, particularly if unacclimatised to heat, often fail to increase intake of salt and water rapidly enough to prevent substantial loss of body fluid, and as a result the blood becomes more concentrated (Keatinge et al, 1986). This can cause a condition known as salt-depletion heat exhaustion, which causes cramps if associated with heavy physical exercise. Similarly, water-depletion heat exhaustion results from dehydration and is characterised by fatigue, nausea, headache and giddiness. More seriously, both conditions make the blood more prone to clot, and this increases the incidence of coronary and cerebral thrombosis in people with pre-existing roughening of the arteries due to atheroma. This is commonly present in middle-aged and older people and accounts for the fact that most of the heat-related mortality from arterial thrombosis occurs in people of these age groups (Donaldson et al, 2003).

31 These adverse effects of thermoregulatory adjustments, rather than lethal overheating of the body, account for the great majority of heat-related deaths in temperate parts of the world, and probably even in tropical regions, but serious overheating of the body can occur in hot climates. Heat stroke describes the syndrome produced by overheating of the body core. It can be produced in normal people by several hours of physical exercise in a hot, humid environment close to or above body temperature. If

heat loss is insufficient, progressive rise in body temperature above 38°C leads to hyperventilation, to cerebral dysfunction involving irritability and confusion, and ultimately to cardiovascular collapse and cessation of sweating (Donaldson et al, 2003). Irritability and headache are important warning signs that body temperature is rising to dangerous levels. The skin is hot and dry and usually red, and rectal temperatures may be 40.5°C or over (NIOSH, 1986). As body temperature rises further, at about 41°C, heat denaturation of proteins causes damage to the large Purkinje cells of the cerebellum and cerebral cortex. Selective damage to brain tissue is therefore found in people who have suffered non-fatal heat stroke (Donaldson et al, 2003). Vascular endothelium, hepatic and renal cells, and striated muscle are then affected, and almost all cells in the body are killed if their temperature rises to 50°C even for a few minutes.

32 Otherwise, heat stroke in sedentary people is usually associated with impairment of sweating and vasodilation, either by drugs or disease (Donaldson et al, 2003). It is most commonly seen in psychiatric patients receiving drugs such as barbiturates or phenothiazines which depress reflex regulation of body temperature generally, or anticholinergic drugs which specifically suppress sweating and vasodilation. General autonomic hypofunction due to diabetes is a common cause of heat stroke in sedentary people. Old age without obvious disability also seems to be associated with increased liability to heat stroke. Diagnosis is suggested by confusion and headache in hot conditions, and confirmed by a deep body temperature close to or above 41°C.

Heat-related mortality of adults at the population level

33 The most important adverse consequence of heat stress is death, and in practice the great majority of excess deaths in hot weather are not due to hyperthermia but to the cardiovascular consequences of heat stress in vulnerable and older people (Donaldson et al, 2003). Older people appear less effective at maintaining normal body temperature compared to younger people, due to declines in sweating and blood flow responses, as well as from decline in the neural control of these responses (Rooke et al, 1994; Anderson et al, 1996). Since these deaths are mostly recorded as due to heart failure, or coronary or cerebral thrombosis, few of the heat-related deaths are specifically attributed to heat in death certificates and national statistics. Accordingly, they can only be assessed by analysis of mortality statistics at the population level.

34 Many studies have shown that in most parts of the world mortality falls to a minimum at a particular environmental temperature, and rises at temperatures above (and below) this value (for reviews see, for example, Kalkstein and Greene, 1997; Martens, 1998; Keatinge et al, 2000; Donaldson et al, 2003). These excess deaths occur mainly in older people. The simplest approach to quantifying this mortality is to identify the temperature band at which mortality is lowest; annual heat-related mortality is then obtained as total excess mortality at temperatures higher than this band. These 3°C temperature bands of minimum mortality are significantly higher in warm regions than in cold regions (Keatinge et al, 2000). In a study spanning Europe, these authors found that minimum mortality is, for example, at 14.3–17.3°C in north Finland, 19.3–22.3°C in London, and at 22.7–25.7°C in Athens. Annual heat-related mortalities per million among people aged 65–74 years (expressed as means and 95% confidence limits) were 304 (126–482) in north Finland, 40 (13–68) in London (which has few days above the minimum mortality band), and 445 (59–831) in Athens.

35 Britain has an unusually low rate of heat-related mortality, but even here total annual heat-related deaths for the whole UK have been estimated to be about 800 per year (Donaldson et al, 2001). These authors noted that such calculations cannot be used directly to quantify mortality that might be produced by internal heating due to RF EMFs, but they imply that any substantial increase in internal heat production will substantially increase mortality in hot weather. Donaldson et al (2003) indicated that, in these circumstances, an additional heat load of around 30% of the normal basal metabolic heat production, ie about 0.4 W kg^{-1}, could not be regarded as a trivial increase, or as safe, but that an additional heat load of around 10%, about 0.1 W kg^{-1}, could be regarded as trivial and therefore safe.

Temperature regulation during pregnancy, in neonates and in children

36 During pregnancy, augmentation of cutaneous blood flow serves to remove heat generated by the increased metabolic demands of gestation (Paul, 1993). Maternal core body temperature at rest increases slightly during the first half of gestation, probably due to the thermogenic properties of progesterone, after which it declines to the non-pregnant level. Recent studies of thermoregulation during moderate exercise under laboratory conditions indicate that pregnant women maintain thermal balance equally as well as non-pregnant women. In a study of women exposed to short-term heat stress in the form of sauna bathing, Vähä-Eskeli et al (1991) found comparable increases in core temperature among non-pregnant subjects and those at 13–14 and 36–37 weeks of gestation. During the recovery period, core temperatures were significantly lower in the late pregnancy group compared with the non-pregnant group, leading the authors to suggest that heat dissipation may even be modestly enhanced during pregnancy.

37 Pathways for the transfer of heat from the fetus to the mother are through the umbilical circulation and through the fetal skin, amniotic fluid and uterine wall. Of these, the umbilical circulation is generally thought to eliminate the bulk (85%) of fetal heat (Power, 1989; Schröder and Power, 1997). As the maternal and fetal blood flows are relatively large and the placenta exposes a large surface area with only a thin barrier, temperature equilibrium is expected to be reached quickly. Fetal temperatures rise quickly if the umbilical cord is occluded, supporting the importance of this site of heat exchange. However, other studies show heat exchange to be less efficient than predicted, probably because of the operation of counter-current heat exchange mechanisms in the vessels of the umbilical cord and perhaps in the smaller vessels in the placenta (Power, 1989; Schröder and Power, 1997). Factors affecting the temperature of the fetus therefore not only include maternal body temperature *per se* but also placental blood flow. There is some evidence to suggest that heat stress from vigorous exercise (Erkkola et al, 1992), heat stress induced by short-term exercise in hypertensive patients (Pirhonen et al, 1994), and fever (Laburn et al, 1992) will all reduce placental blood flow.

38 There is also some evidence suggesting that young infants aged 2–3 months are at an increased vulnerability to heat stress compared with neonates due to their higher metabolic rate, better tissue insulation, and slightly lower surface area to mass ratio (Fleming et al, 1992). In addition, heat stress in young infants may be associated with an increased likelihood of respiratory apnoea. Several studies have indicated that the primary cause seems to be the over-wrapping of infants to protect them from cooler

environmental temperatures (see Donaldson et al, 2003); additional risk factors may include acute febrile illness and an unusually warm or heated environment.

39 The main physical difference between children and adults affecting thermoregulation is the much higher surface-area-to-mass ratio of children. In a warm environment this allows them to rely more upon increased skin blood flow and heat loss through convection and radiation, and less upon evaporative cooling. The lower sweating rate of children is partly due to a lower sensitivity of the sweating mechanism to thermal stimuli. Nevertheless, during exercise in thermally neutral or warm environments, children thermoregulate as effectively as adults. When ambient temperatures exceed body temperature, however, children are more liable to have a higher rate of heat absorption compared with adults. Also, whilst neither children nor adults sufficiently replace fluid loss during exercise in the heat, dehydration may have a more detrimental effect on children because of their greater reliance upon elevated skin blood flow to dissipate heat (Falk, 1998).

Effects of heat exposure on cognitive performance

40 There is increasing evidence that cognitive function can be adversely affected by whole-body heat stress, resulting in increased levels of unsafe behaviour and reduced task performance (see Hancock and Vasmatzidis, 2003). For example, Ramsey et al (1983) found a clear correlation between heat stress and unsafe behaviour in workers in two industrial plants. The increased technological complexity of society has greatly increased the level of mental workload imposed on human operators (Hancock and Meshkati, 1988), which, in turn, increases the propensity for human error. For these reasons, various investigators (NIOSH, 1972; Hancock and Vasmatzidis, 1998, 2000, 2003) have advocated the establishment of criteria for worker exposure to heat stress based primarily on cognitive rather than physiological performance.

41 A large number of volunteer studies have been carried out over the past 40 years. Most have been in laboratory settings where subjects have performed a variety of cognitive tasks during exposure to a series of thermally stressful conditions. These conditions have usually been generated by specifying combinations of environmental temperature, humidity and exposure duration. Overall, it appears that simple tasks, such as reaction time and mental calculations, are less vulnerable to heat stress than more complex tasks, such as vigilance, tracking and multiple tasks performed together (Hancock, 1981, 1982). Similar results can be seen in studies with primates (eg de Lorge, 1983); reduced performance of operant tasks occurs reliably at body temperature elevations of 1°C or more.

42 In humans, Hancock and Vasmatzidis (1998, 2000, 2003) suggested that short-term increases in core body temperature of less than 1°C can be associated with the onset of performance decrement for vigilance, dual and tracking tasks. However, a number of other variables will affect performance of these tasks including the level of skill and acclimatisation of the subjects. In addition, core body temperature rises were not measured in the experiments reviewed but were extrapolated from other data. The precise relationship between increased body temperature and cognitive performance cannot therefore at present be defined (Goldstein et al, 2003); changes in response from small temperature increments would be particularly difficult to judge.

Heat-related disorders are not uncommon in healthy people unaccustomed to hot environments. Heavy exercise either through work or recreation will further exacerbate any problem, particularly if water and salts lost through sweating are not replenished.

Occupational limits on work in hot environments that are based on physiological criteria such as sweat rate, percentage water loss and core temperature recommend that core temperature be restricted to a maximum of 38°C in order to prevent heat-related illnesses.

Cognitive performance will also be adversely affected by a rise in core temperature, susceptibility rising with the complexity of the task to be carried out. However, precise thresholds are difficult to define because of complex interactions with other variables.

The most important adverse consequence of heat stress is death, and in practice the majority of excess deaths in hot weather are not due to hyperthermia but to the cardiovascular consequences of heat stress in older and vulnerable people.

Infants, young children, older people and adults taking certain prescribed medicines and drugs may be particularly susceptible to heat stress.

Effects of heat on the development of the embryo and fetus

43 The majority of studies of effects of RF EMFs on embryo and fetal development were carried out in the 1970s and 1980s. The results of such studies can almost always be attributed to raised internal and/or embryo and fetal temperature (see paragraphs 86–91). The extensive and well-established teratogenic effects of heat on development *in utero* were discussed at a WHO workshop (WHO, 2003a) and are summarised here.

44 Fetal temperature is determined primarily by maternal temperature, since the fetus has almost no ability to regulate its own temperature (Schröder and Power, 1997). Calculation reveals fetal heat production of around 3 W kg^{-1}, about twice the resting heat production of the adult. A temperature difference of around 0.5°C is required to bring the rate at which heat is produced in the fetus into balance with the rate at which it is dissipated to the mother. This close coupling of the fetus to the mother may be regarded as a heat clamp, which effectively prevents the fetus from independently controlling its body temperature before birth. Reduced placental blood flow (see above) could, however, be expected to increase the fetal–maternal temperature gradient and is associated with reduced fetal growth (Edwards et al, 2003).

45 Animal studies have shown that, depending on the extent to which temperature is elevated above normal and the duration of exposure, heat will have either no perceptible effect or will kill pre-implantation stage embryos (Edwards et al, 1995, 2003). Embryos with lethal lesions either will result in an unnoticed pregnancy or might undergo implantation in the uterus and form an early resorption. Surviving embryos treated during pre-implantation go through gestation to form offspring having normal birth weight without an increased incidence of anomalies. Pre-implantation losses are seen for temperature elevations of 1.6 to 1.8°C administered to pigs, sheep and mice for 1 day or more.

46 Hyperthermia during organogenesis induces various developmental defects which can be related to the amount by which maternal body temperature was elevated (Edwards et al, 1995, 2003; Miller et al, 2002). Indeed, the normal body temperatures of some animals are in the teratogenic range for humans. Direct heating *ex vivo* has similar effects. The central nervous system (CNS), which continues to develop in the fetal period and early postnatal life, seems especially vulnerable (Edwards et al, 1995, 2003). Threshold studies have been carried out in experimental rodents. These have examined the incidence of cranio-facial and skeletal defects in mice exposed during early neural tube closure (gestation day 8.5), and microencephaly, reduced cortical thickness and learning defects in mice exposed during neurogenesis, including corticogenesis (gestation days 13–14). Other studies have examined the incidence of cranio-facial and skeletal defects in rats exposed during early and mid-neural tube closure (gestation days 9–10.5). Further studies have investigated microencephaly and other nervous system defects. These include the assessment of changes in learning ability in guinea pigs exposed during early neurogenesis and the formation of the cortical plate (gestation days 20–24). Threshold temperature elevations and dose–response relationships have been identified for cranio-facial and skeletal defects in rats, and microencephaly in guinea pigs. Generally, statistically significant increases in the incidence of heat induced abnormalities are seen in the laboratory at maternal temperature increases of around 2–2.5°C or more, mostly following exposure for tens of minutes up to an hour or so. Higher elevations, up to about 5°C, were required for shorter durations.

47 Some work has been carried out using other species (eg Edwards et al, 1995, 2003). Long-term exposure of pregnant ewes to severe environmental heat during mid- to late-gestation caused severe growth retardation, attributed to reduced maternal appetite, placental circulation, and maternal and fetal endocrine changes. Few studies of the effects of heat on the development of primates have been carried out; a number of teratogenic effects have been reported following repeated elevations of maternal body temperature by about 2.5 to 4.5°C (Edwards et al, 2003).

48 The developing CNS is considered to be the system most sensitive to raised maternal temperature. Microencephaly requires the smallest amount of heat which, in guinea pigs, is engendered by a spike elevation of 2.0 to 2.5°C, rising over a 60-minute exposure period before returning to normal levels. Microencephaly can be induced during neural tube closure and early neurogenesis and, to a lesser extent, during glial cell proliferation and during neuronal myelination, although in the latter case the deficit found at birth is made up during postnatal growth. Interestingly, behavioural deficits were seen in mice and guinea pigs exposed during corticogenesis and additionally in guinea pigs during glial cell proliferation. Generally, however, microencephaly is a marker of gross CNS toxicity and would not necessarily account for minor lesions in specific brain regions, nor abnormal neuronal migration and subsequent abnormalities in dendritic arborisation. Corticogenesis is particularly susceptible to ionising radiation (eg UNSCEAR, 1986) and preliminary studies indicate that it is also sensitive to heat, but few appropriate studies have been carried out. Growth and maturation of the CNS continue after birth in most animal species, including humans; the extent to which increased susceptibility to elevated temperature remains during the postnatal and juvenile period is uncertain.

49 Animal studies have also shown that hyperthermia combined with endotoxins, arsenic, vitamin A, alcohol and aspirin is more effective in causing developmental defects than when administered alone (recently reviewed by Edwards et al, 2003).

50 With regard to the effects of maternal hyperthermia on human *in utero* development, various teratogenic effects have been reported, including neural tube defects such as cranio-facial abnormalities (eg reviewed by Edwards et al, 1995, 2003; Graham et al, 1998). The defects produced generally resemble those found in experimental animals when the hyperthermic episode coincides with the comparable sensitive stage of development, with the CNS being particularly susceptible. Several studies suggest a threshold maternal temperature elevation to about 39°C, a rise of about 2°C above normal, for a significant increase in the incidence of heat induced defects. However, the rigour with which this value has been established is not clear. In addition, possible subtle effects on corticogenesis, which involves processes sensitive to heat such as cell proliferation and migration, have not been explored.

Elevated maternal body temperature during pregnancy can induce various developmental defects in animals. Direct heating of the fetus has similar effects. The CNS seems particularly susceptible, both during early stages such as neural tube closure, and during later stages of early corticogenesis and myelination.

Neural tube defects and microencephaly appear the most sensitive endpoints to have been reported. The effects of elevated maternal temperature on the developing CNS, and particularly on the developing cerebral cortex, have not been fully explored. It is not clear to what extent the increased susceptibility of the developing CNS to raised body temperature continues during postnatal and juvenile growth.

In human studies, similar effects have been reported in the offspring of febrile mothers as well as in the offspring of mothers who used hot tubs or saunas. An increased incidence of neural tube defects was found associated with such episodes in some studies; a threshold of about 39°C has been reported but the rigour with which this has been identified is uncertain.

Thresholds may be lowered in people taking certain medications.

Localised heating

51 The extent to which RF absorption in tissues or organs of the body results in localised peaks of temperature rise in relation to the average rise in core body temperature depends not only on the local SAR but also on the vascularity and flow of blood through the tissue or organ in question. Whilst the former is an intrinsic property of the tissue, the latter can be varied considerably, particularly through the skin and musculature, by metabolic, endocrine and neural control mechanisms (eg Sukkar et al, 2000). Localised heating, for example, usually results in vasodilation and increased blood flow but this response may be compromised by cardiovascular responses to whole-body heating (see paragraphs 25 and 26). The distribution of blood flow through organs and tissues is also likely to be compromised in older people. Whilst cardiac output is maintained in healthy older people, total peripheral resistance is increased (Ferrari, 2002). Cardiovascular diseases that will further compromise the circulation, such as peripheral vascular disease, which may be caused, for example, by atherosclerosis or heart failure, are also highly

prevalent in older people (Corti et al, 2001; De Sanctis, 2001; Lakatta, 2002). In addition, people taking medications such as beta-blockers that affect the peripheral distribution of blood flow may be compromised in this respect. The implication is that heat would be less effectively removed from the tissues of these people.

52 Hyperthermia is being used increasingly as an adjunct to radiotherapy or chemotherapy in the treatment of tumours (Dahl et al, 1999; Falk and Issels, 2001); in addition, localised heating results from the use of ultrasound in clinical diagnosis (Barnett et al, 2000). A considerable number of studies of acute exposure have been carried out both *in vitro* and *in vivo*, investigating 'dose–response' relationships for tissue damage resulting from localised tissue or whole-body heating. Temperatures have usually ranged between 40 and 45°C, sometimes up to 50°C or more, for periods lasting from a few minutes to several hours. The results of such studies have been summarised recently by Dewhirst et al (2003) and, specifically regarding the CNS, by Sharma and Hoopes (2003).

53 In animal studies and in a very small number of human studies (mostly of skin damage), cell loss and/or tissue lesions have been induced in a variety of tissues following whole-body or localised heating. The results from different studies are variable but in many cases lesions occurred when temperatures exceeded 42°C or so for periods of more than about 1 hour (Dewhirst et al, 2003). This occurred with increasing rapidity as temperatures rose further so that at around 45°C, lesions could occur within 10–30 minutes in many tissues. With regard to the susceptibility of different animal tissues, the CNS (including the blood–brain barrier) and the testes seemed the most sensitive to heat; significant changes were reported to occur after exposure to temperatures of only 40–41°C for periods of around 1 hour (Dewhirst et al, 2003). However, human and pig skin seemed less susceptible to raised temperature than the skin of animals such as mice.

54 In contrast to the studies of acute exposure, few chronic studies of heat exposure on different organs or tissues have been carried out. The lens of the eye is regarded as potentially sensitive to RF EMF induced heating because of its lack of a blood supply and consequent reduced cooling ability. In addition, the lens tends to accumulate damage and cellular debris because of a limited capacity for repair. Acute RF heating (more than about 41–43°C for 2–3 hours) can induce lens opacities (cataracts) in experimental animals (see Saunders et al, 1991). However, the threshold for cataract induction resulting from chronic exposure to RF EMFs has not been defined. Historically, cataracts have been associated with chronic, occupational exposure to infrared radiation (eg Lydahl and Phillipson, 1984) indicating that some degree of caution should be exercised with chronic exposure to RF EMFs. Male germ cells in the testis have been known to be heat sensitive for some time; testicular temperatures in most mammalian species are normally several degrees below body temperature (Saunders et al, 1991). Repeated heating of the human testis by 3–5°C will result in a decreased sperm count lasting several weeks (Watanabe, 1959); similar results have been seen in animal studies.

55 Localised tissue damage, which can develop into multi-organ dysfunction, is seen in people who have suffered from acute heat stroke (Donaldson et al, 2003). At about 41°C, heat denaturation causes damage to the large Purkinje cells of the cerebellum and cerebral cortex, resulting in selective brain damage. Vascular endothelium, hepatic and renal cells, and striated muscle are affected at higher body temperatures. Complications

seen in heat stroke patients include acute respiratory distress syndrome, pulmonary oedema, rhabdomyolysis (muscle breakdown), acute renal failure, severe electrolyte disturbances, coagulopathy, disseminated intravascular coagulation, and liver failure.

A number of studies of acute exposure have been carried out on the adverse effects of raised tissue temperature using animals, often in the context of providing guidance on ultrasound use or hyperthermia in clinical practice. Generally, lesions, including those resulting from cell death, occur when tissue temperatures exceed about 42°C for more than about 1 hour.

The CNS and testes appear particularly susceptible to heat induced damage and show significant changes in cell numbers following exposures at 40–41°C and above. These effects are not dissimilar to those seen in acute heat stroke patients, although, here, whole-body heating can lead to multi-organ dysfunction.

Damage to the liver, kidney, vascular endothelium and muscle tissues in heat stroke patients has also been reported; body temperatures may have been in excess of 41°C. In these circumstances however, effects on individual tissues may be confounded by the systemic responses of the whole body to heat.

Few studies have been carried out of the chronic effects of heat on localised tissue damage. Repeated heating of the human testis by 3–5°C results in a decreased sperm count lasting several weeks and similar effects have been seen in animal studies.

The lens of the eye should also be treated as potentially sensitive to heating.

People in whom the function of the cardiovascular system is impaired by disease or medication are likely to be more susceptible to localised heating of tissues than people with normal cardiovascular function.

Other possible effects

56 The increase in personal mobile communications over the last decade has focused attention towards the possible detrimental effects posed by exposure to low level RF EMFs. Particular interest has been expressed that exposure at levels too low to cause significant heating may nevertheless increase the risk of cancer, adversely affect reproduction and development, or impair brain function.

57 These and other possibilities have been much examined and assessed by national and international expert groups. Of particular note are the recent comprehensive reviews by an EC expert group (McKinlay et al, 1996; Veyret et al, 1999), the Independent Expert Group on Mobile Phones (IEGMP, 2000), the Advisory Group on Non-ionising Radiation (AGNIR, 2001c, 2003), the Royal Society of Canada (Krewski et al, 2001a,b), and a French expert group (Zmirou, 2001). Aspects of the literature have also been reviewed by the Health Council of the Netherlands (HCN, 1997, 2000, 2002), STUK (1999), and the British Medical Association (BMA, 2001). The earlier literature was comprehensively summarised by WHO (1993).

Effects on cancer

58 The possibility that low level exposure to RF EMFs may increase the risk of cancer is a major concern and one that has received much attention. Laboratory studies have addressed this possibility using well-established *in vivo* and *in vitro* techniques. The

literature on this topic has been extensively reviewed by McKinlay et al (1996), Brusick et al (1998), Juutilainen and de Seze (1998), Repacholi (1998), Verschaeve and Maes (1998), Moulder et al (1999), and Krewski et al (2001a,b). Recent studies were reviewed by Elder (2003a), Heynick et al (2003), and SSI (2003).

Human studies

59 It is clear that RF EMFs lack sufficient energy to disrupt covalent bonds, so there is no theoretical basis to believe they can cause mutation or other genotoxic effects by affecting DNA directly.

60 However, as with low frequency fields, it has been suggested that exposure to RF EMFs might increase the risk of cancer in humans by decreasing circulating levels of melatonin. While this possibility for low frequency fields has received much attention (see Chapter 4, paragraphs 49–78), very few laboratory studies appear to have explored this likelihood for RF EMFs. Mann et al (1998b) reported that serum melatonin levels were unaffected by night-time exposure to pulsed 900 MHz fields at 0.2 W m^{-2}. Serum levels of growth hormone and luteinising hormone were also unaffected, although cortisol production showed a small, transient increase. Radon et al (2001) reported that repeated exposure for 4 hours to pulsed 900 MHz fields had no effect on salivary concentrations of melatonin, cortisol or selected markers of immune function. Similarly, Bortkiewicz et al (2002) reported that acute exposure to pulsed 900 MHz fields during the evening has no significant effect on urinary levels of 6-hydroxymelatonin sulphate measured up to 12 hours later.

Animal studies

61 A number of studies with rodents have confirmed that RF exposure does not increase mutation rates in somatic or germ cells when temperatures are maintained within physiological limits (IEGMP, 2000). Positive effects reported in some early studies have been attributed to RF EMF induced elevations in temperature (WHO, 1993).

62 However, Sarkar et al (1994) reported large-scale structural rearrangements in DNA in brain and testis cells in mice exposed to 2.45 GHz fields at 0.2 W kg^{-1} for 2 hours per day for up to 200 days. In addition, Lai and Singh (1995, 1996) reported an increased number of single- and double-strand DNA breaks in brain cells rats exposed for 2 hours to continuous or pulsed 2.45 GHz fields at 0.6 or 1.2 W kg^{-1}. DNA was analysed using the alkaline microgel electrophoresis assay. Four hours after exposure to the pulsed fields, the number of strand breaks was increased, while this increase was detected immediately after the exposure using continuous fields. It is possible that these changes somehow involve the production of free-radicals, since these effects were blocked by treatment with melatonin or another free-radical scavenger (Lai and Singh, 1997c). An attempt by Malyapa et al (1998) to replicate the results of Lai and Singh was not successful. Rats were exposed to 2.45 GHz continuous fields for 2 hours at a whole-body SAR of 1.2 W kg^{-1}. No effects on DNA breaks in hippocampal brain cells were seen immediately or 4 hours after exposure. Complementary *in vitro* studies (Malyapa et al, 1997a,b) using 2.45 GHz, 836 MHz or 848 MHz also failed to find any increase in DNA strand breaks. The positive results reported by Lai and Singh were attributed by Malyapa and colleagues to confounding caused by the euthanasia procedure or some unknown aspect of the animal handling.

63 Studies have also been performed using other indicators of DNA damage. Overall, these studies do not suggest that low level microwaves are genotoxic (Brusick et al, 1998; IEGMP, 2000; Krewski et al, 2001a). Some recent animal studies have reported some positive effects (Balode, 1996; Vijayalaxmi et al, 1997a,b; Sykes et al, 2001), although other studies have not (Vijayalaxmi et al, 1999, 2001a). Using the Big Blue mouse model, Takahashi et al (2002) reported a lack of RF EMF induced mutation in the DNA of brain cells.

64 As part of the assessment of the carcinogenic potential of RF EMFs, various studies using rats, mice or rabbits have examined whether long-term exposure to RF EMFs affects longevity and overall health (see WHO, 1993; IEGMP, 2000). Earlier studies tended to use RF EMFs at thermal levels but, even so, few detrimental effects on health or physiological status were reported. Liddle et al (1994) reported the lifespan of mice was shortened by life-long, intermittent exposure to 2.45 GHz continuous fields at 6.8 W kg^{-1}, but not with exposure at 2 W kg^{-1}. The decrease in lifespan was again attributed to the effects of thermal stress. There appear to be no consistent effects of low level RF exposure on the haematopoetic system (Chou et al, 1992; WHO, 1993; Jauchem, 1998). Similarly, significant effects on the immune system have been ascribed to thermal responses or to physiological changes occurring during thermoregulation as a consequence of exposure (IEGMP, 2000). Some recent studies suggest that exposure to low level fields at around 10–20 GHz may increase the production of tumour necrosis factor in peritoneal macrophages of tumour-bearing mice (Fesenko et al, 1999; Novoselova et al, 1999, 2001).

65 Early studies exploring the possibility that RF EMFs might affect spontaneous tumour incidence tended to suffer from insufficient dosimetry, poor histopathology or inadequate follow-up (IEGMP, 2000). Better conducted studies using mice prone to the development of mammary tumours have reported a lack of RF EMF effects (Toler et al, 1997; Frei et al, 1998a,b; Jauchem et al, 2001). La Regina et al (2003) found intermittent long-term exposure of rats to 835 MHz FDMA or 847 MHz CDMA mobile phone signals had no effect on spontaneous tumour incidence in any organ.

66 Repacholi et al (1997) reported that the number of tumours in Eμ *Pim-1* mice exposed to 900 MHz pulsed at 217 Hz was about double that expected in unexposed animals (43% compared to 22%). Animals were exposed twice each day for 30 minutes, from soon after birth until about 18 months old. The SARs were variable and ranged from about 0.008 to 4 W kg^{-1} depending on the age/size of the animals. An attempt to replicate this study using improved dosimetry and pathology with larger numbers of animals failed to confirm these results (Utteridge et al, 2002; see also comments by Utteridge et al, 2003). Exposure for up to 24 months was not associated with any field dependent increase in lymphoma at SARs from 0.25 to 4 W kg^{-1}. Generally, it is very difficult to extrapolate results of such studies using transgenic animals to humans, and the implications for health are far from clear (IEGMP, 2000; Krewski et al, 2001a).

67 The possibility that RF EMFs may act to enhance or promote the growth of tumours caused by other agents has received attention. The effects on standard rodent models of cancer have been tested using a wide range of mobile phone signals and exposure conditions (Wu et al, 1994; Imaida et al, 1998a,b, 2000, 2001; Chagnaud et al, 1999; Bartsch et al, 2001; Heikkinen et al, 2001b; Mason et al, 2001; Anane et al, 2003). No consistent field dependent effects were reported, suggesting exposure does not cause

promotional effects. Similarly, studies investigating spontaneous brain and spinal cord tumours and those induced by prenatal application of chemical carcinogens (Adey et al, 1999, 2000; Zook and Simmens, 2001) have not reported any field dependent increases in tumour numbers or incidence.

68 The possibility that RF EMFs might affect the progression of tumours has been investigated following injection of various types of cancer cells into healthy rats and mice. Positive results in early studies have been attributed to the effects of heat or other coincidental stress (WHO, 1993). Other studies using both continuous and pulsed signals suggest that exposure does not affect survival time or enhance the growth of tumours (Santini et al, 1988; Salford et al, 1997; Higashikubo et al, 1999).

69 A few studies have investigated if RF EMFs affect circulating melatonin levels. Stärk et al (1997) measured melatonin levels in the saliva of cattle in the vicinity of a short-wave radio transmitter and found no chronic effects, although a possible short-term rise was noted. Vollrath et al (1997) found that short-term exposure of rats at night or during the day to continuous or pulsed 900 MHz fields at 0.06–0.36 W kg^{-1} had no effect on pineal melatonin synthesis. Similar results were seen in Djungarian hamsters exposed at 0.04 W kg^{-1} and Heikkinen et al (1999) found no effects on melatonin production in mice chronically exposed to pulsed or continuous 900 MHz fields at 0.35-1.5 W kg^{-1}. Imaida et al (1998a,b) reported repeated, daily exposure to 929 MHz and 1.5 GHz fields for 6 weeks increased day-time serum melatonin levels in rats.

70 Using a microgel electrophoresis assay, Lai and Singh (1997c) reported that subcutaneous injection of melatonin (1 mg kg^{-1}) immediately before and after RF exposure blocked any field induced increases in DNA single- and double-strand breaks in brain cells of a rat. Animals were exposed for 2 hours to pulsed 2.45 GHz (2 μs, 500 pulses per second) at an average whole-body SAR of 1.2 W kg^{-1}. Similar blocking effects were reported using the spin-trap compound, N-tert-butyl-alpha-phenylnitrone.

71 Changes in heat shock (*hsp*) gene expression following exposure to low level RF EMFs have been investigated using a transgenic nematode worm, *Caenorhabditis elegans*. This nematode model carries the bacterial *lacZ* reporter gene downstream of the promoter of the *hsp16* gene. When these nematodes are exposed to conditions that would stimulate expression of heat shock protein, they produce β-galactosidase (the product of the *lacZ* gene) which can be readily assessed. This model has been used for both aquatic and soil-based toxicity testing. It has been reported that exposure of *C elegans* to 330 or 750 MHz fields for 2–16 hours at 0.5 W elevated expression of *hsp* genes, suggesting that exposure induced protein damage in these nematodes (Daniells et al, 1998). The SAR was estimated at 0.001 W kg^{-1} (de Pomerai et al, 2000a). There were no detectable increases in temperature of either the worms or the culture medium – the increase in reported gene activity was considered equivalent to a 3°C increase in temperature. In addition, it was further reported that growth rate and development into egg-bearing adults was significantly increased by overnight exposure at 0.5 W, and this growth increase was sustained for 24 hours after cessation of exposure (de Pomerai et al, 2000b, 2002). Increased expression was also reported in a preliminary study which used the signals from a digital mobile phone handset to expose these worms for 7 hours (de Pomerai et al, 1999). These phenomena merit further study and independent replication; the implications for human health also need careful consideration (see French et al, 2001).

Cellular studies

72 Many cellular studies have investigated the possibility that exposure to RF EMFs may induce biological changes that may be relevant to the causation or development of cancer. As with studies using animal models, a wide variety of cell types, endpoints and exposure conditions have been employed. Overall, the results of these studies are somewhat mixed, and most reported effects appear to be relatively modest in the absence of significant heating. These particular studies have been comprehensively reviewed by several expert groups, including IEGMP (2000) and Krewski et al (2001a,b), and most recently by Meltz (2003).

73 In general, results from a number of experiments (summarised by WHO, 1993; Brusick et al, 1998; Krewski et al, 2001a) do not provide convincing evidence that RF EMFs are genotoxic. Consistent with many studies indicating that exposure to various RF EMFs does not cause mutation, Gos et al (2000) reported that mutation rate in yeast was unaffected by exposure to 900 MHz fields at SARs of 0.13 or 1.3 W kg^{-1}.

74 Several studies have measured the potential of RF EMFs to induce DNA damage *in vitro* using the alkaline microgel electrophoresis assay to measure the incidence of DNA strand breaks. No consistent field dependent effects have been reported using various mouse or human cell lines exposed to a variety of frequencies and modulations, mostly associated with mobile phone technologies (Malyapa et al 1997a,b; Vijayalaxmi et al, 2000; Li et al, 2001; Miyakoshi et al, 2001; McNamee et al, 2002a,b; Tice et al, 2002). In these studies, cells were exposed from 0.6 W kg^{-1} for 24 hours to 100 W kg^{-1} for 2 hours.

75 Other studies have explored the effects of RF EMFs on indirect measures of DNA damage. Effects on chromosomal aberrations have been well investigated. Results are mixed but many studies suggesting positive effects have been criticised for confounding due to potential thermal effects (IEGMP, 2000). Better conducted, more recent studies using human lymphocytes have not reported any field dependent effects (Vijayalaxmi et al, 1997c, 2001b,c; Maes et al, 2001). Effects on sister chromatid exchange have also been explored. In a preliminary study, Khalil et al (1993) reported increases in sister chromatid exchange in human lymphocytes exposed to 167 MHz, but no field dependent effects have been reported using 2.45 GHz at 75 W kg^{-1} (Maes et al, 1993), or using GSM fields around 900 MHz at up to 10 W kg^{-1} (Maes et al, 1995, 1997, 2001). Further studies have explored effects on micronucleus formation and, again, results are mixed (IEGMP, 2000). Some studies using mobile phone signals did not report any effects on human lymphocytes (Vijayalaxmi et al, 2001b,c), human leukocytes (McNamee et al, 2002a,b; Tice et al, 2002) or mouse fibroblasts (Bisht et al, 2002). A negative result was also reported using human lymphocytes exposed to 2.45 GHz (Vijayalaxmi et al, 1997c). In contrast, increases in micronuclei formation have been reported in human lymphocytes following exposure to the mobile phone signals (D'Ambrosio et al, 2002; Tice et al, 2002) and to 2.45 or 7.7 GHz fields (Maes et al, 1993; Zotti-Martelli et al, 2000).

76 Although there is a lack of consistent evidence to suggest that exposure to RF EMFs has a direct carcinogenic effect, some studies have investigated whether RF EMFs may act synergistically with known mutagens or promoting agents to enhance their effect.

77 Early studies reported enhancement of latent cellular transformation by 2.45 GHz fields following exposure to x-rays or benzo[a]pyrene (Balcer-Kubiczek and Harrison, 1985, 1991), although the effect was not replicated using 836 MHz fields (Cain et al, 1997). Similarly, amplification of the genotoxic effects of mitomycin-C reported by Scarfi et al (1996) and Maes et al (1997) are in contrast to earlier negative results using chemical carcinogens (see IEGMP, 2000). Pakhomov et al (1997) reported exposure to 61 GHz fields at thermal levels could enhance DNA recombination in yeast cells exposed to ultraviolet radiation (UVR). In a recent study of neoplastic transformation, Roti Roti et al (2001) exposed C3H 10T½ mouse fibroblasts to FDMA-modulated 835 MHz or CDMA-modulated 847 MHz fields for 7 days at 0.6 W kg^{-1}. The cells were also irradiated with 4.5 Gy of x-rays. No increases in neoplastic transformation were reported following exposure to RF EMFs either alone or in conjunction with x-rays.

78 Calcium ions play an important role in many cell signalling pathways. Various studies have investigated the effects of RF EMFs on calcium ion movement across the cell membrane, particularly in brain tissues. IEGMP (2000) concluded that that the evidence for an RF-dependent effect was contradictory, although the possibility that such effects may occur with amplitude-modulated signals was considered intriguing.

79 The advent of fluorescent dyes specific for calcium ions has made the real-time estimation of intracellular calcium concentrations in individual cells possible. Utilising a specific fluorescent dye, Cranfield et al (2001) exposed human Jurkat cells to a continuous or pulsed 915 MHz field for 10 minutes at 1.5 W kg^{-1}. No consistent effects on mean calcium levels were detected in individual cells, nor were there significant changes in the percentage of cells showing calcium spikes, spike height or number of spikes. The single significant field dependent change observed may be attributable to chance.

80 Studies investigating the effects of RF exposure on the expression of early response genes, such as *c-fos* and *c-jun*, have produced inconsistent results (Ivaschuk et al, 1997; Goswami et al, 1999).

81 Other studies have also reported field dependent changes in heat shock proteins. Kwee et al (2001) exposed transformed human epithelial cells to 960 MHz for 20 minutes at 0.002 W kg^{-1} and found increased levels of hsp70, but not hsp27. Leszczynski et al (2002) reported an increase in hsp27 in human endothelial cells exposed to a 900 MHz field for 1 hour at an average SAR of 2 W kg^{-1}. The number of phosphoproteins including hsp27 was transiently increased more than three-fold following exposure. However, statistical analysis of these results was not presented. Tian et al (2002) found effects of 2.45 GHz on *hsp70* expression in glioma cells using SARs above 20 W kg^{-1} even when thermal effects were taken into account. While interesting, replication and confirmation of these studies are needed before any conclusions can be drawn.

82 Natarajan et al (2002) investigated the effect of high peak power pulsed fields on nuclear factor kappa B protein, an important regulator of DNA transcription. Human monocytes were exposed to 8.2 GHz for 90 minutes. The average SAR was 10.8 W kg^{-1} but 10% of the cells could have been receiving 22 to 29 W kg^{-1}. An almost four-fold increase in nuclear factor kappa B activity was observed, which was considered to be likely due to thermal effects.

83 Finally, increased cell proliferation may play a role in carcinogenesis. The studies investigating whether RF EMFs increase cell proliferation have generally produced mixed results (IEGMP, 2000; Krewski et al, 2001a).

84 Ornithine decarboxylase (ODC) is an enzyme whose activation is related to cell proliferation. Most, but not all, tumour promoters increase ODC activity. Transient changes in ODC levels and activity have been reported in mouse fibroblasts exposed to 835–915 MHz fields amplitude-modulated at between 16 and 60 Hz for several hours at 2.5 W kg^{-1} (Byus and Hawel, 1997; Penafiel et al, 1997). Earlier studies reported field dependent effects in human melanoma and two other cell lines using amplitude-modulated 450 MHz fields at 0.08 W kg^{-1} (Byus et al, 1988; Litovitz et al, 1993). No changes in ODC activity were seen using frequency-modulated or unmodulated fields. However, all the field dependent changes were relatively modest compared to those induced by established tumour-promoting substances (IEGMP, 2000). No additional *in vitro* studies appear to have investigated this phenomenon further. Stagg et al (2001) found that acute exposure of rats to a pulsed 1.6 GHz field at up to 5 W kg^{-1} did not affect ODC levels in brain tissues. Regarding other enzyme systems, too few studies have investigated potential RF EMF influences to formulate conclusions (Pashovkina and Akoev 2000; Ivanov et al, 2001; Seaman et al, 2002).

85 Some studies have reported modest increases in proliferation (Cleary, 1997; Stagg et al, 1997) but other studies have reported either no effects (Gos et al, 1997) or decreases in cell growth (Kwee and Raskmark, 1998). Using 835 MHz FDMA-modulated signals or 847 MHz CDMA-modulated signals, Higashikubo et al (2001) reported that exposure of mouse fibroblasts, C3H 10T½ cells, or human glioma cells at 0.6 W kg^{-1} for up to 100 hours had no field dependent effects on cell cycle parameters, including transit time through G1, G2, and S phase, and the probability of cell division. Wang et al (2001) demonstrated an inhibition of proliferation and induction of apoptosis in nasopharyngeal carcinoma cells exposed to 42.2 GHz at a power density of 1 mW cm^{-2} for 30 minutes each day for 4 days.

There is no direct experimental evidence to suggest that RF EMFs may significantly increase the risk of cancer.

Melatonin levels in humans do not appear to be affected by exposure to RF EMFs although very few studies have investigated this possibility. The evidence from animal studies is more equivocal.

Well-performed animal studies clearly show that long-term RF exposure does not promote the development of specific mammary cancers, colon tumours, lymphomas or liver cancers. Nor does exposure appear to increase the development of specific brain and spinal cord tumours, or to affect the progression of injected tumours. While a few animal studies have reported field dependent effects, some of these can be criticised for poor experimental techniques and others may have little relevance to human health.

The majority of cellular studies do not suggest RF EMFs can affect indicators of DNA damage or repair. However, reports of field dependent increases in the expression of heat shock genes in the apparent absence of heating justify further study.

Thus while the results of many laboratory studies strongly indicate the absence of any increased risk of cancer, some caution still needs to be exercised since it is not possible to dismiss all possibilities.

Reproduction and development

86 The possibility that RF EMFs may affect fertility, reproduction, and development has been much investigated. Experimental studies have been reviewed by Jensh (1997), Verschaeve and Maes (1998), O'Connor (1999) and Krewski et al (2001a), and most recently considered by Heynick and Merritt (2003) and AGNIR (2003).

87 Overall, there is no convincing scientific evidence that exposure to low level RF EMFs can affect reproduction and development in mammals – where consistent effects have been reported they can be attributable to thermal insults induced by exposure. Hyperthermia is an accepted teratogen and exposure of pregnant animals to RF EMFs sufficient to induce elevations of maternal temperature will cause a hierarchy of responses that depend on the magnitude and duration of the rise in temperature. These responses range from subtle behavioural changes in offspring and growth retardation, to gross morphological changes and increased intrauterine deaths (Saunders et al, 1991; Edwards et al, 2003).

88 Testicular temperatures in mammals are normally several degrees below that of the rest of the body, and exposure to heat, from RF EMFs (or other sources) can induce temporary sterility. Recently, Khillare and Behari (1998) reported that male fertility could be decreased by prolonged exposure to 200 MHz fields, modulated at 16 Hz at about 2 W kg^{-1}. However, modest warming may explain these effects (IEGMP, 2000).

89 Studies investigating whether RF EMFs potentiate the teratogenic effects of chemicals and solvents suggest complex interactions can occur but only using fields at hyperthermic levels (Nelson et al, 1997a,b, 1999, 2001; Cheever et al, 2001).

90 In a small study, Magras and Xenos (1997) reported that exposure to the various fields from a commercial antenna park produced a rapid drop in fertility in mice. Twelve male and female mice were caged outdoors close to the antenna park or in a nearby village. Exposures ranged between 1.7 and 10 mW m^{-2}. The animals were mated five times over six months. It was found that the litter sizes were small compared to those of animals living in an RF EMF free environment in a laboratory. The last mating away from the antenna park did not restore litter size. The lack of a concurrent control group, however, undermines these results, and the possibility that the observed changes were the result of other stresses in the environment cannot be discounted.

91 Two studies have examined the behavioural consequences of prenatal (and early postnatal) exposure to RF EMFs. Cobb et al (2000) exposed pregnant rats to ultrawideband microwave pulses (300 ps rise time, 1.8 ns pulse width, average whole-body SAR 0.045 W kg^{-1}) for 2 minutes per day from day 3 to 18 of gestation (and from postnatal day 1 to 10). Offspring were examined using an extensive battery of developmental landmarks and functional and behavioural tests, including water maze performance and operant response. No significant exposure-dependent effects were found except on three metrics (less vocalisation in exposed males, longer medial-to-lateral length of hippocampus, and lower mating frequency but without change in mating success). The lack of a consistent aetiology suggested these differences were attributable to chance. Bornhausen and Scheingraber (2000) exposed freely-moving pregnant rats to pulsed 900 MHz fields continuously from day 1 to 20 of gestation. Whole-body SAR (of dams) ranged from 0.00175 to 0.075 W kg^{-1}. Subsequent operant performance of offspring was assessed as adults using three differential schedules of reinforcement requiring either high or low rates of responses – exposure had no effect on task performance.

Although there are few informative studies, the available scientific data do not suggest that exposure to RF EMFs at levels found in the environment poses any significant threat to reproduction or development. One study suggesting that low level exposure decreases fertility in mice contains severe methodological flaws.

Neurobehavioural effects

92 The brain and nervous system have long been considered sensitive targets for the effects of exposure to low level RF EMFs. Various claims have been made over many years suggesting that RF EMFs from a variety of civilian and military sources may cause adverse changes in an assortment of behavioural or neurological functions. These include lack of concentration, poor memory, changes in sleep pattern, as well as loss of appetite and reduced libido. Together these symptoms have sometimes been called the neurasthenic or microwave sickness syndrome. More recently, exposure to mobile phones has been suggested to cause similar effects.

93 These possibilities have been much investigated in respect of a variety of endpoints using a wide range of exposure conditions. The earlier literature was reviewed by WHO (1993), while more recent studies have been considered by Hermann and Hossman (1997), Pakhomov et al (1998), D'Andrea (1999), IEGMP (2000), Krewski et al (2001a,b), Zmirou (2001), Hamblin and Wood (2002), Sienkiewicz (2002) and D'Andrea et al (2003a,b).

Human studies

94 Due to the close proximity of the head to a mobile phone handset in normal use, the tissues and structures within the head may absorb relatively greater amounts of energy than is absorbed elsewhere in the body. Specific concerns have been expressed about possible adverse effects on memory, attention or other cognitive functions.

95 The detrimental effects of mobile phone use on driving performance have been comprehensively reviewed by IEGMP (2000). Impairments in speed or accuracy of reaction to changing road circumstances have been clearly identified. However, as these do not appear to be primarily caused by exposure to RF EMFs, they are not considered further here.

96 *Subjective symptoms* A wide range of subjective symptoms has been attributed to exposure to various sources of RF EMFs both at home and at work. Some users of mobile phones report they suffer a variety of subjective complaints, including headaches and migraines, fatigue, skin itches, and sensations of warmth (Frey, 1998; Hocking, 1998; Chia et al, 2000; Hocking and Westerman, 2000; Sandström et al, 2001; Santini et al, 2002). Less commonly reported symptoms include dizziness, blurred vision, memory loss, confusion and vagueness, toothaches, and nausea. Prosaic explanations for some of these symptoms may exist (Sandström et al, 2001).

97 In a single-blind study, Koivisto et al (2001) presented 48 normal individuals with either real or sham exposure to a pulsed 902 MHz field. Subjects were asked to rate subjective symptoms and sensations during these sessions. No significant differences were found between exposure conditions, although fatigue and headaches increased toward the end of sessions.

98 In a double-blind study, Hietanen et al (2002) exposed 20 volunteers who reported themselves to be sensitive to RF EMFs to analogue or digital mobile phone signals. Blood pressure, heart rate and breathing rate were measured every 5 minutes and subjects were asked to report any abnormal feelings. Nineteen of the subjects reported symptoms, most of which were sensations in the head of pain or warmth. However, more symptoms were reported during sham exposure than real exposure, suggesting the possibility that the blinding conditions between treatments were not adequate. The physiological parameters showed no relevant trends, although they tended to decrease throughout the day.

99 In another double-blind study, Zwamborn et al (2003) explored the effects of exposure to GSM and UMTS signals on self-reported well-being. Small, but significant, field dependent effects with UMTS signals were seen in a group of subjects who had previously reported complaints attributed to GSM fields and in a control group who had not reported any complaints. No effects were seen using GSM signals either at 900 or 1800 MHz. An explanation based on thermal effects seems unlikely: the maximum SAR in the head was calculated to be in the region of 0.07 mW kg^{-1}.

100 *Cognitive performance* Several recent studies have examined the effects of RF EMFs associated with mobile phone use on attention, memory and other cognitive functions. Overall, these studies only provide weak evidence that subtle changes in cognitive performance may occur following exposure at levels below those recommended by ICNIRP (1998) for general public exposure. The underlying effects may be thermal and result from very small, localised heating of the brain in the areas beneath the phone.

101 Preece et al (1999) used a copy of a commercial phone with an output of 1 W, and found that exposure to an analogue 915 MHz field for about 30 minutes significantly decreased choice reaction time. Non-significant changes were observed using digital signals. Simple reaction times were unaffected and there were no changes in word, number or picture recall, or in spatial memory. The changes in choice reaction time were attributed to an improvement in synaptic function within the angular gyrus or to a facilitation of neuronal transmission caused by localised heating.

102 Koivisto et al (2000a) used a digital phone with an output of 0.25 W, and found that exposure to 902 MHz fields significantly decreased response times in simple reaction time and vigilance tasks. In addition, the time needed to accomplish a mental arithmetic subtraction task was decreased during exposure. Memory tasks were not examined in this study. The changes were attributed to localised heating effects exerting a facilitating effect on cognitive processing in the prefrontal cortex and parietal cortex, especially in those tasks that require attention or cognitive manipulation in working memory. A further study (Koivisto et al, 2000b) using a task where the working memory load was varied, found that exposure again speeded up reaction time, but this effect was only significant when the memory load was particularly demanding. However, an attempt by the same group to confirm and extend these results was not successful (Haarala et al, 2003). Using an improved experimental design, no consistent field dependent effects were observed on reaction times or error rates during the performance of a battery of nine cognitive tasks. This suggests that the results of the original study should be treated with some caution.

103 Other studies have reported RF EMF effects broadly consistent with the original results of Koivisto et al or Preece et al, although all of these suffer problems in method or interpretation which challenge their usefulness. Zwamborn et al (2003) reported a diffuse and inconsistent pattern of field dependent effects on a range of different cognitive tasks following very low level, whole-body exposure to GSM and UMTS fields. Lass et al (2002) reported that exposure to a 450 MHz field modulated at 7 Hz improved performance of a recognition memory task. Edelstyn and Oldershaw (2002) found that exposure facilitated cognitive tasks involving attentional capacity and in one task which involved processing speed. Smythe and Costall (2003) reported a field dependent improvement in immediate memory in male subjects exposed to an 1800 MHz field: no effects on memory were seen after about 7 days, or in female subjects at either time. Lastly, a mild facilitating effect on attention, as measured in paper and pencil tests, was reported by Lee et al (2001) in adolescent users of mobile phones. Attempts to replicate these results would be most useful.

104 *Electrical activity of the brain* Using the fields associated with mobile phones, most recent electrophysiological studies have failed to find an effect of pulsed RF EMFs on the spontaneous, awake electroencephalogram (EEG) (Roschke and Mann, 1997; Hietanen et al, 2000). However, under more demanding experimental conditions, such as during the performance of memory tasks, possible field dependent effects have been noted. For example, Freude et al (1998, 2000) reported effects of pulsed 916 MHz fields on slow brain potentials at right, central and temporo-pariental regions during a visual monitoring task. Eulitz et al (1998) also found a decrease in spectral power in the bands 18.75–31.25 Hz during an auditory discrimination task. The effect was only present when subjects processed task-relevant target stimuli and was not present for irrelevant standard or novel stimuli. It was also found to be specific to the side of the brain directly exposed to the field. Similarly, in narcoleptic patients, Jech et al (2001) reported effects on two specific components of the EEG evoked by the presentation of rare (oddball) stimuli on the right half of the visual field.

105 EEG changes have been reported in healthy volunteers exposed to pulsed 902 MHz fields during performance of either an auditory task (Krause et al, 2000a) or a visual memory task (Krause et al, 2000b). Both of these studies found that exposure affected the 8–10 Hz band of the EEG which has been associated with attentional demands (Klimesch et al, 1992). This suggests that RF EMFs may have effects on the cortical oscillatory systems mediating cognitive processes such as attention (Krause et al, 2000a). Croft et al (2002) reported effects on event-related desynchronisation during an auditory discrimination task and on resting EEG parameters from a 900 MHz GSM handset operating in 'listening' mode producing an average power of 3–4 mW.

106 *Sleep* The normal, cyclic variations in the functional state of the brain, which occur during sleep, can be examined and quantified using the EEG. A number of recent studies have used these techniques to examine the effect fields associated with mobile phones may have on sleep.

107 An initial report by Mann and Roschke (1996) indicated that exposure to pulsed 900 MHz fields at night decreased the latency to sleep onset. There was also a reduction in the duration and percentage of rapid eye movement (REM) sleep, and an increase in

spectral power density during REM sleep. However, these results could not be repeated in subsequent studies using a circular antenna exposure system (Wagner et al, 1998, 2000). Borbely et al (1999) found that the intermittent exposure to a GSM-like signal affected the spectral power in the non-REM sleep, with a maximal rise in the 10–11 Hz and 13.5–14 Hz bands of the EEG. REM sleep and sleep onset latency remained unaffected. Lebedeva et al (2001) found that overnight exposure caused a decrease in the percentage of slow-wave sleep.

108 Results obtained by Huber et al (2000, 2002) suggest that acute exposure during waking may affect the subsequent EEG pattern during sleep. Using a pulsed 900 MHz signal from a mobile phone, exposure at a peak SAR of 1 W kg^{-1} increased the spectral power in the 9.75–11.25 Hz and 12.5–13.25 Hz bands of the EEG in non-REM sleep. The effects persisted, but were maximal during the initial part of sleep. Exposure during continuous wave fields was without significant effect. Changes in cerebral blood flow were also measured in the dorsolateral prefrontal cortex following exposure.

109 *Cardiovascular function* Changes in cardiovascular function are unlikely to occur in the absence of thermoregulatory responses (Jauchem, 1997; Black and Heynick, 2003). Early reports from the former Soviet Union suggesting that occupational exposure to RF EMFs may affect heart rate and reduce blood pressure have been attributed to chance variation (IEGMP, 2000). Mann et al (1998a) reported that the control of heart rate was not affected by exposure at night to the fields from a mobile phone.

110 However, in a small study Braune et al (1998) reported that both systolic and diastolic blood pressure of volunteers was increased by about 5 mm Hg by exposure for 35 minutes to the signals from a GSM mobile phone held close to the right ear. Heart rate was slightly lowered by exposure. Since capillary perfusion in the hand was decreased, it was concluded that exposure had increased vasoconstriction, possibly as result of changes to sympathetic activity originating within the brainstem. However, these effects were not replicated in a subsequent, more extensive study by Braune et al (2002). This study also addressed the criticisms of Reid and Gettinby (1998) on the design of the original study. Slow increases in blood pressure were again noted, but these were independent of RF exposure. In addition, there were no field dependent changes in serum levels of norepinephrine, epinephrine, endothelin and cortisol, which affect vasomotor tone.

Laboratory studies with volunteers have only recently begun to investigate the effects that low level exposure to the fields associated with mobile phones may have on the brain and behaviour. To date, only subtle and transient effects have been reported and any implications for health remain unclear.

The available data are too limited to decide if exposure can cause headaches or other subjective symptoms.

There is some evidence that acute exposure may cause mild facilitation effects on attentional processes, and decrease reaction times to stimuli, possibly as a consequence of localised heating of brain tissues. The possibility that the magnitude of the effect increases with the complexity of the task used is unclear.

Effects on sleep have been reported but remain less well defined. No consistent changes have been seen on cardiovascular function.

Animal studies

111 The possible effects of microwaves on the brain and behaviour have been studied in animals using a range of methods and techniques, from changes in specific gene expression in cells, to investigations of changes in learned behaviours. These studies have been reviewed by Hermann and Hossman (1997), Pakhomov et al (1998), and D'Andrea (1999). RF EMF effects on learning and memory have been considered by Lai (2001).

Gene expression

112 A few studies have investigated if the induction of stress-related genes and their proteins increase following exposure to RF EMFs. These genes respond to various insults, such as ischemia or hyperthermia, and help to minimise potential damage. Mickley et al (1994) exposed rats to 600 MHz fields at 9.3 W kg^{-1} and measured increased *c-fos* protein expression in various areas of the forebrain, especially in cortical and periventricular areas. These changes were blocked by an opioid antagonist and were considered consistent with opioid-mediated stress. In another study, rats exposed to high peak power ultrawideband pulses (0.25–2.5 GHz) at a peak electric field of 250 kV m^{-1} for 2 minutes did not show any changes expression of *c-fos* protein levels (Walters et al, 1995). Body temperatures of the animals in this study rose by less than 0.5°C.

113 Fritze et al (1997a) exposed the heads of rats to simulated GSM signals (890–915 MHz pulsed at 217 Hz) at 7.5 W kg^{-1} and measured changes in the messenger RNAs of *hsp70*, *c-fos*, *c-jun*, and GFAP using *in situ* hybridisation histochemistry. Only changes consistent with brain hyperthermia or immobilisation stress were found either immediately or 24 hours after exposure. Seven days after exposure, no changes were observed in the levels of the relevant proteins. Similarly, Morrissey et al (1999) reported that local exposure of the head of mice to a 1.6 GHz Iridium satellite phone signal (pulse modulated at 11 Hz with a duty cycle of 4 : 1 and a pulse duration of 9.2 ms) for 1 hour only significantly increased *c-fos* expression in the forebrain when the average SAR in the brain exceeded 4.3 W kg^{-1}. The pattern of *c-fos* change was consistent with a thermal stress, thermoregulatory activity, and the effects of restraint. There were no differences between continuous and pulsed exposures. Stagg et al (2001) exposed rats for 2 hours to 1.6 GHz Iridium signals using a head-only exposure system that produced local SARs in the brain of up to 5 W kg^{-1}. No significant increases in body temperature were recorded and no field dependent increases in *c-fos* and *c-jun* mRNA were observed.

Blood–brain barrier

114 The blood–brain barrier (BBB) serves to protect the brain from potentially harmful compounds and helps to regulate and control the fluid environment of the brain cells. About 20 years ago several studies reported that low level exposure to RF EMFs may alter the permeability of the BBB and cause leakage of molecules from the blood into the cerebrospinal fluid. Such responses could produce severe and lasting consequences. However, better controlled studies failed to replicate these findings and the original observations were ascribed to various confounding factors (see Blackwell and Saunders,

1986). Consistent changes in the BBB were only found when physiologically significant heating was induced (using SARs of more than about 7 W kg^{-1}).

115 However, some recent studies have again suggested that low level RF exposure may affect the BBB. Neubauer et al (1990) reported that significant changes occurred with exposures above 2 W kg^{-1} for 30 minutes or more. Persson et al (1997) reported changes that varied with both modulation frequency and SAR. Any changes appeared largely independent of SAR for continuous fields, whereas there appeared to be an inverse relationship between effect and SAR for pulsed fields. SARs of around 0.01 W kg^{-1} produced more than twice as many pathological changes than SARs of 2–8 W kg^{-1} which may have produced heating. In an extension of this work, Salford et al (2003) reported that brief exposure of juvenile rats to 915 MHz fields caused long-lasting neuronal damage throughout the brain, and especially in the cortex, hippocampus and basal ganglia. Animals were exposed for 2 hours at SARs of 0.002, 0.02 and 0.2 W kg^{-1} and damage was reported to increase with increasing SAR. However, there are a number of caveats with the study and major reservations regarding the results. These include not only the modest size of study (n = 8/group) and a rather wide age range of the rats used (12–26 weeks of age), but also serious uncertainties about the metrology and dosimetry. The quantification of damaged neurons was also highly subjective, and too few data were presented to justify any conclusions. Overall, replication using improved methods and with tighter control of experimental variables is necessary before any extrapolation can be made regarding potential human health effects.

116 In contrast, other recent studies have failed to confirm these changes on albumin permeability using either single or repeated exposure (Fritze et al, 1997b; Tsurita et al, 2000; Finnie et al, 2001, 2002). Exposure at thermal levels only induced modest and transitory changes in the BBB. In addition, none of these well-conducted studies reported any morphological changes in brain tissues.

Electrical activity

117 The electroencephalogram (EEG) is a description of the spontaneous, slow electrical activity of the brain and can be used to indicate subtle changes in brain function. Exposure to very low levels of amplitude-modulated fields has been reported to alter the EEG of the brain in cats and rabbits (see WHO, 1993).

118 Complex changes in spectral power of various bands of the EEG have been reported in recent studies using rodents, rabbits and cats (Thuroczy et al, 1994; Chizhenkova and Safroshkina, 1996; Pu et al, 1997; Vorobyov et al, 1997; Ivanova et al, 2000). However, differences in experimental and exposure conditions preclude making general conclusions on these data, although some of the changes appear to reflect thermal responses.

Neurotransmitters

119 Changes in various neurotransmitter systems have sometimes been reported in a number of isolated studies from different laboratories. Many of these data were reviewed by Hermann and Hossman (1997) who ascribed many of the reported changes to spurious temperature effects.

120 An extensive series of experiments from one laboratory suggests that exposure to low level RF EMFs may affect cholinergic function in a time-dependent fashion (Lai, 1992). Both pulsed and continuous 2.45 GHz fields could elicit decreases in cholinergic activity. The threshold with pulsed fields (0.45 W kg^{-1}, specific absorption per pulse of 0.9 mJ kg^{-1}) was approximately equal to the rat's auditory perception threshold. It was reported that similar changes in cholinergic function could be induced by stressors such as noise and acute restraint, suggesting that exposure may be associated with mild stress. In addition, exposure was found to increase the concentration of benzodiazepine receptors in the cortex following acute but not repeated exposures (Lai et al, 1992a), again suggesting an anxiety or stress response. More recent studies have provided evidence on the involvement of endogenous opioids (Lai et al, 1992b) in the medial septal nucleus (Lai et al, 1996). Recently, Testylier et al (2002) reported that acute exposure to RF EMFs may cause sustained decreases in acetylcholine release from the rat hippocampus.

121 Mausset et al (2001) reported that exposure to 900 MHz fields reduced the GABA content in the Purkinje cells in the rat cerebellum. Animals were exposed to pulsed fields at 4 W kg^{-1} and continuous fields at 32 W kg^{-1}, suggesting the possibility of thermal effects.

Learned and other behaviours

122 Many data indicate that changes in many well-learned behaviours occur only when core temperatures are increased by about 1°C or more (WHO, 1993). Under some circumstances, ongoing operant behaviours can be terminated completely above a threshold corresponding to a whole-body SAR of about 4 W kg^{-1}. Many factors are known to modify this value, however, including the frequency of the applied field, the ambient temperature and relative humidity, and the animal size and species.

123 This heating effect is illustrated by the results of a behavioural study using rats exposed to microwaves at 600 MHz (Mickley et al, 1994). Significant deficits in the performance of a working memory task were observed when exposures caused rises in rectal and brain temperatures of at least 1°C. These changes were correlated with an increase in expression of the *c-fos* gene in the cortex.

124 However, results of some recent studies appear to challenge this conclusion (see also D'Andrea, 1999). Lai et al (1994) reported that the behaviour of rats performing a test of spatial memory function in a radial arm maze was severely disrupted by daily exposure for 45 minutes to pulsed 2.45 GHz fields at 0.6 W kg^{-1}. Exposure did not cause a measurable rise in colonic temperature but acquisition was retarded and exposed animals consistently made more errors than controls. Additional results suggested that exposure had activated the endogenous opioid systems and so caused a decrease in cholinergic activity within the hippocampus. In an earlier experiment, Lai et al (1989) reported that exposure for 20 minutes improved learning for the first 2 days, although final performance and overall accuracy were not affected.

125 Wang and Lai (2000) placed rats in a Morris water maze immediately after being exposed to pulsed 2.45 GHz fields at 1.2 W kg^{-1} for 1 hour. The animals had to learn to escape from the water by locating a submerged (non-visible) platform. Exposed animals took longer to find the platform than control animals throughout the training

sessions, and, in contrast to the control animals, spent much time trying to climb the side walls of the maze. In a probe trial without the platform being present, the exposed animals were reported to have spent less time swimming in the quadrant of the maze that should have contained the platform. Therefore, it was concluded that exposure had disrupted spatial reference memory functions and that the exposed animals had to use other, less efficient, learning strategies to locate the platform. However, statistical analysis of the probe trial data by one-way analysis of variance revealed no significant treatment effect, and only post hoc analysis suggested a statistical difference between the exposed and control animals (see also IEGMP, 2000).

126 In contrast, Sienkiewicz et al (2000) found that that exposure of mice for 45 minutes to pulsed 900 MHz fields at 0.05 W kg^{-1} had no significant effects on performance in a radial arm maze. Animals were tested immediately after exposure or following delays of 15 or 30 minutes. The animals tested without delay took longer to complete the task, possibly due to some mild stress associated with exposure. Similarly, Dubreuil et al (2002, 2003) exposed rats to pulsed 900 MHz fields for 45 minutes using a head-only system before daily testing on various spatial memory tasks (performed using a radial arm maze or a dry land version of the Morris water maze) or on an object recognition task. No consistent effects on the performance of any task were seen using average SARs in the brain of either 1 or 3.5 W kg^{-1}. In addition, a recent attempt by Cobb et al (2004) to replicate the study of Lai et al (1994) failed to confirm any field dependent effects on task performance in a radial arm maze. As in the original study, rats were exposed using a circularly polarised waveguide to pulsed 2.45 GHz fields at 0.6 W kg^{-1} for 45 minutes before daily learning trials in a radial arm maze.

127 The hippocampus slice preparation has been much used in neurophysiology to study mechanisms associated with memory. Using a novel parallel plate waveguide, Tattersall et al (2001) exposed slices of rat hippocampus to 700 MHz continuous fields at SARs of between 0.0006 and 0.0044 W kg^{-1}. Changes were found in the electrically evoked field potential in CA1 that depended on the magnitude of the SAR – low field intensities produced an increase in the amplitude of the population spike by up to 20%, but higher intensity fields produced either increases of up to 120% or decreases of up to 80%. In addition, it was reported that exposure at about 0.0011 W kg^{-1} reduced or abolished drug induced epileptiform activity in 36% of slices tested. Any field induced rises in temperature were too small be detected even using sensitive measuring equipment. Imposed temperature changes of up to 1°C failed to mimic the effects of the RF EMFs.

128 In a preliminary study, Löscher and Käs (1998) ascribed behavioural and postural abnormalities observed in a herd of dairy cows to the fields from a nearby TV and mobile phone transmitter site. However, the lack of concurrent sham-exposed animals to control for the possible impact of environmental or other factors renders any interpretation premature.

The eyes

129 The eyes have long been considered sensitive to the effects of localised increases temperature, although exposure to RF EMFs must be both prolonged and intense to

cause lasting detrimental effects (WHO, 1993, see also Saito et al, 1998). The effects of RF fields on the eyes have been reviewed by Elder (2003b).

130 A series of earlier studies (summarised by Kues and Monahan, 1992) has indicated that localised exposure of the eyes of anaesthetised monkeys to pulsed 2.45 GHz (10 μs duration at 100 pulses per second) at an SAR in the eye of 2.6 W kg^{-1} (specific absorption of 26 mJ kg^{-1} per pulse), or more, for several hours resulted in lesions in the corneal endothelium (Kues et al, 1985). The vascular leakage from the blood vessels of the iris was increased. Lesions in the cornea were also induced by exposure to continuous fields at 2.45 GHz, but were less effective compared to pulsed fields. Topical pretreatment with the ophthalmic drug timolol maleate appeared to reduce the threshold for these effects to 0.26 W kg^{-1} (Kues et al, 1992). Intermittent exposure over a 10 week period resulted in early degenerative changes in the retina, which were also exacerbated by application of timolol maleate.

131 In contrast, Kamimura et al (1994) were unable to induce corneal, lenticular or retinal lesions in the eyes of unanesthetised macaque monkeys exposed to continuous (but not pulsed) 2.45 GHz fields at levels exceeding the threshold for continuous field induced corneal damage described by Kues et al (1985). The technique used for the identification of corneal lesions (specular microscopy) was the same as that used by Kues et al (1985); the latter authors, however, used histological techniques to confirm damage to both the cornea and retina, in contrast to Kamimura et al (1994).

132 More recent studies using 1.25 GHz high peak power pulsed fields did not report signs of retinal degeneration or functional impairment in the eyes of rhesus monkeys intermittently exposed over a 3 week period at average SARs in the retina of 4 W kg^{-1} (Lu et al, 2000). However, some evidence of mild injury was seen using average SARs of 8.4 and 20.2 W kg^{-1}. Similarly, no signs of ocular damage were observed in rabbits or monkeys exposed to continuous 60 GHz fields at 10 mW cm^{-2} for either a single 8 hour exposure or five separate 4 hour exposures (Kues et al, 1999).

The possibility that exposure to RF EMFs may affect neurobehavioural function in animals has been explored from a number of perspectives using a wide range of exposure conditions.

There are sporadic reports of field dependent effects but none has been firmly established.

The least questionnable evidence for low level effects relates to the changes in cholinergic and opioid activity using whole-body SARs of about 1 W kg^{-1}, although the possibility that some of these changes may be due to increases in stress or anxiety associated with field exposure should be considered. Field induced changes in cholinergic function might predict effects on learning and memory but the evidence for such effects is conflicting. Results of two studies from one laboratory showing performance deficits using pulsed 2.45 GHz fields were not confirmed in two independent studies using GSM signals. Changes in excitability of hippocampal slices *in vitro* following exposure to very weak fields requires independent verification.

Nevertheless, the possibility that low level exposure may engender behavioural or cognitive changes in animals under certain circumstances cannot be ruled out – too few tasks and exposure conditions have been examined to formulate definitive conclusions at this time.

Biological uncertainties

133 The effects of heat in healthy adults, through physical work and/or in warm, humid environments, is well documented and understood; many volunteer studies have been carried out. However, the distribution of heat sensitivity in the general population is less well documented. In general, people with certain medical conditions and/or those taking medication are not eligible in volunteers experiments. These restrictions are also usually applied to older people, children and pregnant women. With regard to RF EMF induced whole-body heat loads, there is some uncertainty regarding the identification of tolerable heat loads in people with varying susceptibilities to heat, and the way in which these might be modified by physical activity and inclement environmental conditions.

134 Increasingly, people work in jobs requiring astute cognitive processing. In many cases, the safety of others depends on the mental alertness of the operator. A large number of studies have been carried out of the effects of elevated environmental temperatures on cognitive performance; it is generally agreed that more cognitively demanding tasks are more susceptible to heat induced performance decrements than simple mental tasks. However, such effects also depend on other factors, such as training, as well as ergonomic factors. The susceptibility of cognitive tasks to heat load, and to raised body or brain temperature, and ways in which other environmental variables affect susceptibility, are yet to be clearly identified.

135 There is compelling experimental evidence that raised maternal body temperature will adversely affect pregnancy outcome. The central nervous system (CNS) seems particularly susceptible and in this respect neural tube defects and microencephaly have been reported in a number of studies. However, possible effects on the development of the cortex, known to be particularly susceptible to other harmful agents, and the behavioural consequences of these effects on the nervous system have not been fully explored. There is some evidence that the risk of effects such as neural tube defects is increased in the offspring of women who experience hyperthermia during pregnancy, particularly during the first trimester, but the rigour with which this has been established is less certain. In addition, it is not clear to what extent the increased susceptibility of the developing CNS to raised body temperature continues during infancy and early childhood.

136 With regard to localised heating of parts of the body, thresholds for tissue necrosis resulting from acute exposure to heat have been identified using animal studies in a number of different tissues. The thresholds for such effects are less clearly identified in humans. In addition, the cumulative effects in tissues that might result from repeated exposure are less clear. The long-term consequences of functional change induced by elevated tissue temperatures, in endocrine glands, or in parts of the brain such as the pituitary or hypothalamus, are also not fully understood. Further, the impact of disease, particularly of the cardiovascular system, on a person's ability to dissipate excess heat from organs and tissues is not well established.

137 The results of other experiments suggesting that low level RF EMFs may induce adverse biological responses are beset with uncertainty, limiting their practical usefulness as a basis for establishing exposure standards. This uncertainty originates from several sources. Firstly, studies may have been performed with inadequate

scientific rigour, and have deficiencies in experimental design and lack control of potential artefacts. Other studies may have inadequate metrology or dosimetry. Studies may have inappropriate or incorrect data analysis or have insufficient statistical power to detect small effects. Finally, there is the acknowledged uncertainty of extrapolating results to living humans from data obtained using various animal species and *in vitro* experimental models.

138 As with studies using EMFs, the general inconsistency in reported effects and the lack of attempts to replicate results are major sources of uncertainty. This applies to studies reporting effects as well as to studies reporting their absence. Further, the view that some responses may only occur with specific frequencies or pulsed modulations makes broad generalisations difficult, if not impossible, to draw. The appropriateness of using SAR as an exposure metric for non-thermal interactions has also been questioned.

139 Finally, other uncertainties result from an incomplete understanding of the distribution of sensitivity to RF EMFs amongst the population, particularly age-related differences and those resulting from medical conditions or treatment.

Summary

140 Heat-related disorders should be avoided in the majority of normal healthy adults, provided that core body temperature does not rise above 38°C. This is likely to prevent adverse effects on the performance of all but the most demanding cognitive tasks. High rates of physical activity and/or warm, humid environments will reduce the additional RF heat loads that most adults can tolerate without exceeding 38°C. An RF heat load of 0.4 W kg^{-1} averaged over the whole body should be sufficiently low that these other factors can be ignored.

141 Individual susceptibility to heat-related disorders varies considerably in the general population. Older people, and infants and children may be considered particularly susceptible. In addition, adults taking certain drugs and other chemicals that have direct effects on the control of body temperature, or on metabolism or heat production of the body may also be considered at greater risk. An RF heat load of 0.1 W kg^{-1} averaged over the whole body should be physiologically trivial in this context.

142 Exposure of pregnant women to an average whole-body SAR of 0.1 W kg^{-1} should not result in adverse effects on the development of the embryo and fetus *in utero*. The fetus itself is thought to be in general about 0.5°C above maternal body temperature (the embryo less so) and is to some extent limited in its ability to dissipate heat to the mother by heat exchange within the umbilical blood vessels. In view of the uncertainty regarding possible effects of raising fetal temperatures directly through the absorption of RF EMFs, a rise in embryo and fetal temperature to less than 38°C should also not result in adverse developmental effects. The development of some tissues, such as the CNS, continues during infancy and early childhood, suggesting that some potential increased susceptibility may continue during these periods.

143 With regard to localised heating and the susceptibility of individual tissues to heat, the CNS, the testis and the lens of the eye seem particularly sensitive, the last more through a limited ability to dissipate heat than a greater sensitivity to heat *per se*. Other tissues, such as liver, kidney and muscle, seem marginally less susceptible, but nevertheless can also be adversely affected by elevated temperature. Temperature rises in the CNS (ie the brain, retina and spinal cord) to above 38°C, of the other tissues

of the neck and trunk (with the exception of the testes) to above 39°C and of the tissues of the limbs to above 40°C may result in localised heat induced damage. The testes are particularly sensitive to the effects of heat; adverse effects should not occur in this tissue provided temperature increases are less than 1°C.

144 The ability to dissipate heat from locally heated tissues or regions of the body will depend on their temperature in relation to their surroundings and rate of flow of blood through the tissue. Both may to some extent be compromised by significant whole-body heating when the increase in skin blood flow is greater than the corresponding increase in cardiac output. In addition, people with cardiovascular disease, such as peripheral vascular disease or heart failure, which will reduce the circulation of blood through tissues, may be at increased susceptibility to localised heating of tissues by RF EMFs compared with people with normal cardiovascular responses.

145 In addition, a number of studies suggest that low level RF EMFs may induce a variety of subtle biological responses. Of particular note are possible effects of pulsed fields on brain function and on changes in heat shock protein expression. Further work is needed to examine these and other possibilities, especially to consider if local heating effects may explain these results. Overall, none of these possible effects is considered sufficient to provide a coherent framework on which to base quantitative restrictions for human exposures.

The most plausible and coherent set of data from which guidance can be developed concerns raised temperatures and the physiological stress induced by increased heat loads. In addition, these data show 'dose–response' relationships. A cautious approach has been used to derive thresholds for adverse health effects that are scientifically robust.

Other studies reviewed lack plausibility, coherence and consistency precluding a positive role in this process.

Heat-related disorders should be avoided in the majority of normal healthy adults, provided that core body temperature does not rise above 38°C. High rates of physical activity and/or warm, humid environments will reduce the additional RF heat loads that most adults can tolerate without exceeding this rise in body temperature. An RF heat load of 0.4 W kg^{-1} averaged over the whole body should be sufficiently low that these other factors can be ignored.

Some people are potentially susceptible to heat-related disorders. These include older people, infants, children pregnant women and other adults taking certain medications. In addition, the performance of cognitively demanding tasks may also be vulnerable to increases in heat load or body temperature. An RF heat load of 0.1 W kg^{-1} averaged over the whole body should be physiologically trivial in this context.

With regard to partial-body heating, temperature rises in the head, spinal cord, embryo and fetus above 38°C; in other tissues of the neck and trunk (with the exception of the testes) above 39°C; and in the limbs above 40°C, may result in localised heat induced damage.

The testes are particularly sensitive to the effects of heat. Adverse effects will not result from temperature increases less than 1°C.

People in whom the function of the cardiovascular system is impaired by disease or medication are likely to be more susceptible to localised heating of tissues than people with normal cardiovascular physiology.

DOSIMETRY

146 Computational dosimetry provides a link between external non-perturbed EMFs and the fields induced within the body. This gives guidance to the choice of reference levels in relation to basic restrictions.

147 Basic restrictions on SAR prevent whole-body heat stress and excessive localised tissue heating.

148 The state-of-the-art approach to deriving reference levels is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic models of the body. Subsequent sections describe the calculations of whole-body averaged SAR and localised SAR in the wrist and ankle.

149 Techniques for performing temperature calculations in the body are described and recent results for each type of exposure, from whole-body to highly localised exposure of vulnerable organs such as the eye and brain, are reviewed.

SAR calculations

Computational methods

150 The Finite-Difference Time-Domain, FDTD method (Taflove, 1995), provides a direct solution of the coupled, time-dependent Maxwell curl equations and is ideally suited for application to voxel phantoms. The method follows the time evolution of the propagation, reflection and absorption of electromagnetic waves in a domain comprising the target and surrounding space. The domain is divided into a three-dimensional lattice of cells that are assigned discrete electrical properties. The components of the electric field, $\boldsymbol{E}$, are positioned on the middle of the edges and the components of the magnetic field, $\boldsymbol{H}$, are at the middle of the faces of the lattice cells. An explicit second-order finite-difference procedure then leap-frogs, evaluating $\boldsymbol{E}$ from $\boldsymbol{H}$ and vice versa at alternate half-time steps until equilibrium has been reached. A domain enclosing the target and a boundary condition on the surface of the domain must be chosen to mimic numerically the unbounded region outside the domain by absorbing the outgoing scattered waves. The perfectly matched layer (pml) based boundary conditions of Berenger (1994) can produce a very small reflection from the boundary. The technique is based on splitting the electric and magnetic fields into two in the absorbing boundary region. This gives additional degrees of freedom for the specification of material parameters. Thus it is possible to create a non-physical absorbing medium, adjacent to the external mesh boundary, in which waves of arbitrary frequency and angle of propagation are caused to decay rapidly while maintaining the velocity and impedance of the media from which they propagated.

151 The Finite Integration Technique, FIT (Weiland, 1990), constitutes a slightly different conceptual approach to that of FDTD, but both approaches lead to the same basic numerical scheme.

Calculations of whole-body averaged SAR

152 The FDTD method has been applied (Dimbylow, 1997a) to the NRPB voxel phantom (NORMAN) to provide a comprehensive set of whole-body averaged SAR values for adult, 10-, 5- and 1-year-old phantoms, grounded and isolated in air from

1 MHz to 1 GHz for plane wave exposure. It was not then computationally tractable to perform FDTD calculations directly at a cell size of 2 mm. Therefore, the phantom was rescaled to produce 6 mm, 1 cm and 2 cm models with the properties of the rescaled cells being taken as the volume average of the basic component voxels. As the frequency increases, smaller cell sizes are required so that an adequate sampling of the waveform is performed. The computational effort required is proportional to the reciprocal of the fourth power of the cell size. Computing technology has now advanced to the point where the FDTD calculations can be performed at the basic 2 mm resolution of NORMAN. This enables the SAR values to be performed over discrete tissue types avoiding the smearing out of tissue properties in calculations with larger rescaled voxels. The reduction in the voxel size also allows SAR to be calculated at higher frequencies.

153 Calculations of the whole-body averaged SAR have been performed (Dimbylow, 2002) from 100 MHz up to 3 GHz by using the basic resolution of NORMAN, around 2 mm. At lower frequencies a 4 mm resolution discrete voxel version was used with an overlap to 200 MHz and it was found that the whole-body averaged SAR was a robust quantity with respect to model resolution. The adult phantom was resampled to represent the heights and masses of reference 10-, 5- and 1-year-old children (ICRP, 2002) whilst retaining the 2.077 mm voxel resolution at the higher frequencies and 4 mm at the lower frequencies. The reference 10-year-old has a height of 1.38 m and a mass of 33 kg, the 5-year-old has a height of 1.1 m and a mass of 20 kg and the 1-year-old has a height of 0.75 m and a mass of 10 kg. The whole-body resonance occurs at around 65, 85, 110 and 155 MHz for the adult, 10-, 5- and 1-year-old phantoms under isolated conditions. The resonance occurs when the height of the body is approximately $\lambda/2$, where λ is the wavelength in air. When the phantom is grounded, the reflection in the ground plane halves the resonant frequency. However, the body is not a thin dipole and the exact resonant frequencies depend on the anatomy and values of the frequency-dependent dielectric properties. Under grounded conditions the whole-body resonance occurs at around 35, 50, 65 and 95 MHz for the adult, 10-, 5- and 1-year-old phantoms. In general, the basic restriction on whole-body averaged SAR is the critical condition requiring the lowest external field value.

154 Chen and Gandhi (1989) calculated whole-body averaged SAR values from 20 to 100 MHz in the previous Utah 'half-inch' body model derived from slices in an anatomical atlas. They used a resolution of 2.62 cm. These were continued from 100 to 915 MHz (Gandhi et al, 1992) at a resolution of 1.31 cm. Tinniswood et al (1998) looked mainly at the power deposition in the head and neck but also reported whole-body averaged SAR values. Calculations were performed either at the $2 \times 2 \times 3$ mm^3 basic resolution of the Utah anatomical phantom near resonance or at the lower $6 \times 6 \times 6$ mm^3 resolution version away from resonance. The Gabriel et al dielectric parameters were used and calculations were performed from 10 to 350 MHz (Gabriel, 1996; Gabriel et al, 1996a–c). The predicted resonance frequencies of 35 MHz for grounded and 60 MHz for isolated conditions agree well with the NRPB calculations (Dimbylow, 2002). The calculated resonant SAR values are 94.8 and 74.9 μW kg^{-1} per V m^{-1} rms for grounded and isolated conditions. The corresponding values from Dimbylow (2002) are 93.1 and 81.2 μW kg^{-1} per V m^{-1}, differences of +2 and –8%.

155 Mason et al (2000) calculated whole-body SAR from 70 to 2000 MHz at 3 and 5 mm resolution in the Brooks digital anatomical man model for isolated conditions. At 70 MHz, using the 3 mm version, the predicted value is 71.6 $\mu W\,kg^{-1}$ per $V\,m^{-1}$, whilst at 2000 MHz the value is 14.9 $\mu W\,kg^{-1}$ per $V\,m^{-1}$. The corresponding values from Dimbylow (2002) are 80.0 and 15.6 $\mu W\,kg^{-1}$ per $V\,m^{-1}$, differences of –10 and –4%.

Localised SAR

156 The maximum of the induced layer current occurs in the lower limbs for exposure of the body to a plane wave EMF at frequencies below and around the whole-body resonance. The ankle region has a narrow cross-section with little high conductivity muscle. The sections comprise mainly low conductivity bone and fat. Consequently, there is a channelling of the current through the high conductivity muscle, which produces high, localised SAR values in the muscle. It is not computationally tractable to perform FDTD calculations, at the basic 2 mm resolution, at frequencies below 100 MHz. The localised SAR averaged over 10 and 100 g in the lower limb has been calculated (Dimbylow, 1997b) for a unit current injected through the open upper boundary of a partial leg model using a finite-difference solution of the quasistatic potential equation from 0.1 to 80 MHz. The bottom 220 slices of the whole-body model, NORMAN were extracted to make a voxel model of the lower leg.

157 The localised SAR averaged over 10 and 100 g in the lower arm has been also been calculated (Dimbylow, 2001) as a function of the current injected through the open upper boundary of the arm model. This consists of 147 slices from NORMAN, extending from a plane through the hand at the 'knuckles' to just below the elbow.

158 The ICNIRP guidelines give limb current reference levels of 100 and 45 mA for occupational and general public exposure between 10 and 110 MHz to provide compliance with basic restrictions on localised SAR. The limb current reference level provides a conservative limitation on the localised SAR, in both the arm and the leg, calculated using NORMAN.

159 There has been interest in the deposition of energy in the head from mobile phones. Examples of FDTD calculations of localised SAR from the coupled transceiver-head geometry can be found in Dimbylow and Mann (1994), Bernardi et al (1996), Okoniewski and Stuchly (1996) and Watanabe et al (1996).

160 Gandhi et al (1996) looked at energy absorption in the head from $\lambda/4$ and $3\lambda/8$ monopoles at 835 and 1900 MHz. They used the $1.875 \times 1.875 \times 3\ mm^3$ Utah model of the adult head and reduced-scale versions to represent 10- and 5-year-old children. They found that the 1 g SAR peak value was larger for the smaller models of the children, particularly at 835 MHz. It was also found that the relative penetration of energy into the deeper anatomical structures of these smaller models was more noticeable because they were nearer the source. However, these findings were contradicted by the work of Schonborn et al (1998). They used the FIT code MAFIA (CST, 1994). Simulations were performed using head phantoms based on MRI scans of an adult (voxel size of $2 \times 2 \times 1\ mm^3$) and two children ($2 \times 2 \times 1.1\ mm^3$) of ages 3 and 7 years. Differences in absorption were investigated at 900 and 1800 MHz using 0.45λ dipole sources. The results revealed no significant differences in the absorption of EMFs between MRI-based phantoms of both adults and children and for various linearly scaled adult phantoms.

Thermal dosimetry

Computational methods

161 The thermal effects of EMFs may be gauged by the distribution of temperature rises within the body. Thermal dosimetry aims to determine these, and to relate them to other metrics such as SAR or power density. As frequency increases, the penetration depth of the fields decreases. At frequencies above about 10 GHz, most of the energy is absorbed within the first few millimetres of tissue, and the temperature rise is well correlated to the incident power density. At lower frequencies, the SAR is a better predictor. There is no clear-cut frequency at which SAR ceases to be a useful metric; there is a transitional region in which both metrics are useful but neither is perfect. ICNIRP (1998) has chosen 10 GHz as the crossover point between restrictions on SAR and on power density.

162 The most appropriate computational technique depends on the exposure conditions. In circumstances where the whole body is exposed at a level which causes elevation of the core temperature and consequent thermoregulatory responses, coarsely segmented models of the whole body have been used with some success (eg Stolwijk, 1970; Charny et al, 1987). The trunk, head and each limb are divided into a few segments, and each segment is then divided into layers, which are assumed to be of homogeneous composition (eg skin, fat, muscle, bone). A single temperature is taken to be representative for each region, and heat capacities and transfer coefficients are 'lumped'. The advantages of such a model are computational efficiency and the relatively small number of parameters which need to be determined experimentally. Central and local thermoregulation can be incorporated in these models. However, these models are inappropriate when exposure is highly non-uniform.

163 The progress of models for whole-body exposure has not been as rapid as that for localised or regional exposure. The reason is probably that a comprehensive and accurate thermal model of man would require precise knowledge of thermoregulation and thermal properties of every organ. Such parameters can only be obtained by human experimentation, and the number of measurable quantities is not sufficient to solve uniquely for the large number of unknown parameters in a whole-body model.

164 Most theoretical studies of localised or regional heating use some variant of the heat equation. This is a partial differential equation which describes the variation of temperature $T(\mathbf{r},t)$ as a function of position $\mathbf{r}$ and time t. It is obtained by considering an infinitesimal volume element and equating the rate of change of thermal energy within it to the total heat flowing into it. In its traditional form, the 'Pennes bioheat equation' (Pennes, 1948) takes the form:

$$\rho c\frac{\partial T}{\partial t}=\nabla.(k\nabla T)+\rho Q+\rho S-\rho\omega\rho_{\mathrm{b}}c_{\mathrm{b}}(T-T_{\mathrm{b}}) \qquad (1)$$

where ρ is the density, c the specific heat capacity and k the thermal conductivity of the tissue at $\mathbf{r}$; the subscript 'b' indicates the corresponding parameters for blood, Q is the power generated per unit mass by metabolic processes, S is the specific energy absorption rate (SAR), and ω is the blood perfusion rate.

165 The Pennes equation has the great virtue of simplicity. Heat transfer between tissue and blood is represented by a heat sink term, and only one parameter ω is needed to

describe the blood flow within each tissue. However, it was originally derived on the assumption that heat transfer mainly takes place in the capillary beds. It has since been shown to the contrary that the principal site of heat exchange is between the terminal arterial branches and the pre-capillary arterioles (Chen and Holmes, 1980). Other authors have replaced the heat sink term with an enhanced effective conductivity (Weinbaum and Jiji, 1985), modified the heat sink term with an efficiency factor (Brinck and Werner, 1994), or introduced an explicit description of the vasculature (Kotte et al, 1996). However, comparison with these more recent models shows that for many applications the traditional Pennes bioheat equation is still a valid approximation.

166 Continuum-based models such as the Pennes equation and its variants are partial differential equations, and must be discretised before they are solved. The most widespread discretisation methods are the finite-difference methods and finite-element methods. Finite-difference methods are computationally simple, but require calculation of temperatures on a uniform rectilinear grid. Finite-element methods may utilise non-uniform grids; these can model complex geometries more accurately and sometimes improve computational efficiency.

Heating of the skin

167 At frequencies greater than about 10 GHz, absorption of electromagnetic energy takes place mostly in the skin and other superficial tissues. For dosimetric purposes superficial absorption has certain simplifying features. When the penetration depth of the field is small compared with the radius of curvature of the body surface, one-dimensional models of electromagnetic propagation and heat transfer may be used.

168 Blick et al (1997) have measured threshold incident power densities for perception of microwaves and millimetre waves spanning frequencies from 2.45 to 94 GHz as well as infrared radiation. They found that thresholds in the microwave region decrease with increasing frequency, and that thresholds at 94 GHz were similar to those for infrared radiation.

169 Riu et al (1997) have developed a thermal model for human thresholds of microwave-evoked warmth sensations. Based on examination of the experimental data by Blick et al (1997), they concluded that the observed data were consistent with the hypothesis that perception is triggered by an increase in skin temperature in the region 0.06–0.08°C. The measured threshold power densities P_{th} (in mW cm^{-2}) approximately fit the curve

$$P_{th} \approx \frac{100}{f^{0.68}} \qquad (2)$$

where f is the frequency in gigahertz. The observed frequency dependence of the threshold is due to the variation in penetration depth, although this is mitigated by thermal conduction which plays an important role.

170 A further volunteer study of millimetre wave exposure at 94 GHz was performed by Walters et al (2000). In a sample of ten volunteers they found the mean threshold of pain at 1.25 W cm^{-2}, corresponding to an increase in surface temperature of 9.9°C from a baseline of 34.0°C to a threshold temperature of 43.9°C during a 3 second exposure. In the same study, infrared thermography was used to measure the subjects' skin

temperature as a function of time. This was then fitted to a simple one-dimensional thermal model to determine the energy transmission coefficient and penetration depth of the field. The energy transmission coefficient is the fraction of the incident power density which penetrates the skin surface; the penetration depth is the depth at which the transmitted power density has been reduced by a factor 1/e. The experimental values of these parameters were consistent with the dielectric properties of skin tabulated by Gabriel (1996). There was, however, a considerable scatter between experiments and subjects, presumably due in part to variation between individuals, particularly in skin water content.

RF contact burns

171 Threshold currents for perception and pain were determined experimentally by Chatterjee et al (1986), from measurements on 367 adult human subjects. Based on the two areas used for finger contact (25 and 144 mm^2), the authors suggest that the variation of threshold current with contact area is consistent with a model that predicts proportionality with the fourth root of area. For finger contact with an area of 25 mm^2, the average threshold for perception in the male population rises with frequency from about 4 mA at 10 kHz to over 40 mA at 100 kHz, and then stays approximately constant up to 3 MHz. Pain thresholds are no more than 50% greater than those for perception. There appears to be a systematic difference in average thresholds between the male and female population, the thresholds for males being 1.26 times those for females. Assuming that the mechanism of perception is a threshold SAR causing a sensation of warmth in the hand or wrist, the threshold current is proportional to the square of the body dimensions; accordingly the authors predict the values for 10-year-old children should be 60% of those for adults.

172 Foster and Erdreich (1999) used a simplified spherically symmetric thermal model to estimate the threshold current for painful heating. Since the current density and SAR depend on the size of the electrode, this is a critical parameter. For a 1 mm electrode and a frequency of 1 MHz, they estimated a threshold of 8 mA. They were able to make only limited comparison between the model and the available measured data (Chatterjee et al, 1986; Hocking and Joyner, 1992) due to lack of sufficient experimental data given by those studies. A major source of uncertainty is the distribution of current density beneath the electrodes.

Thermal response times

173 Using simple one-dimensional thermal models it is possible to identify the thermal time constants pertaining to heat conduction and convection by blood flow (Foster et al, 1998; Foster and Erdreich, 1999). These constants determine the time taken for the temperature to approach a steady state after the source of exposure is switched on or off. This is an appropriate averaging time for dosimetric purposes. An effective time constant can be determined by combining the effects of conduction and convection; conduction dominates for small heated regions (less than a few centimetres), and convection for larger regions. Since the field penetration depth varies with frequency, so does the time constant. The authors discussed the relationship between the time constants and the size of the heated region or penetration depth. The decreasing trend

of time constants with frequency from 10 to 300 GHz has been accommodated in national and international standards and guidelines (IEEE, 1992; NRPB, 1993; ICNIRP, 1998) by a similar variation in averaging time over that frequency range.

Heating of the eye

174 The eye is a particularly sensitive organ for several reasons. Since the blood flow within the inner tissues is negligible, one of the major cooling mechanisms is absent. With prolonged exposure the proteins of the lens can suffer permanent damage leading to a loss of transparency (cataract). Experimental results using rabbits suggest that the threshold for cataract formation is a temperature rise of 3–5°C (eg Guy et al, 1975). The geometry of the eye, and the discontinuity of the dielectric constants between the eye and the bony orbit, are such that standing waves may be set up so generating a localised temperature rise.

175 Most theoretical studies have usually simulated exposure to a plane wave, a nearby dipole antenna, or various approximations to a mobile phone. Since the average mass of the adult human eye is 7.5 g (ICRP, 2002), the SAR average over the whole eye is close to the average over the 10 g region recommended by ICNIRP, and many authors have chosen to compute the former value. In general, the most significant value in these computations is the temperature rise within the lens. The calculated temperature rises are usually greater for the cornea, but due to the natural gradient of temperature as a function of depth, the absolute temperature is likely to remain less in the cornea than in the lens.

176 Mokhtech et al (1994) mapped the SAR within the eye exposed to the near-field of a dipole antenna at mobile phone frequencies (840, 915, 1500 and 1800 MHz). Peak SARs were almost twice as high at 1500/1800 MHz as at 840/915 MHz. A localised temperature rise was found to occur in the vitreous humour just behind the lens. The bioheat equation was used to estimate temperature rises, and their dependence on the distance of the antenna from the eye was investigated. Antennas were assumed to be radiating at the power limits specified in the C95.1 standard (IEEE, 1992) for the 'uncontrolled environment', namely

$$P_{\mathrm{r}} = 1.4\left(\frac{450}{f}\right) \qquad (3)$$

where P_{r} is the radiated power in watts and f is the frequency in MHz. Temperature rises were predicted to reach 2.7°C for an antenna 5 mm from the eye, and 0.5°C for an antenna at the 'exclusion distance' 25 mm from the eye. In the latter case the 1 g averaged SAR could reach 6 W kg^{-1}.

177 Hirata et al (1999) calculated SAR and temperature rise for plane-wave exposure at 0.6–6 GHz using FDTD and the Pennes bioheat equation. They found several resonant frequencies, the strongest being at 1.9 GHz. Some of these resonances were found to correspond to identifiable standing wave patterns in the eye (whose mass is about 10 g) or the head. There was a fairly strong correlation between the SAR averaged over the whole eye and the maximum temperature rise within the eye. The temperature rise is not simply proportional to the SAR, however, because the tissue dielectric properties

are frequency dependent. At resonance the incident power density 10 W m^{-2} was found to produce an average SAR of 0.36 W kg^{-1} and a temperature rise of 0.14°C; at 6.0 GHz these fell to about 0.2 W kg^{-1} and 0.075°C.

178 After further development of their model, Hirata et al (2000) found slightly different results. An additional peak at 1.0 GHz not seen in the earlier results was attributed to coupling of weak resonances in the eye and head. In the later paper the trend of maximum temperature was to *increase*, rather than decrease, with frequency, with the temperature peak at 1.9 GHz being much reduced. The discrepancy is most probably due to the introduction in the later work of a convective heat transfer term to represent heat loss to the blood perfusing the choroid. At 6.0 GHz the results are similar to those of the earlier paper, since most energy is deposited in the anterior part of the eye where heat loss is dominated by convection at the cornea. An incident power density of 50 W m^{-2} was calculated to produce an SAR of 1.1 W kg^{-1}, and temperature rises up to 0.28°C in the lens and 0.33°C in the cornea. At frequencies above this, heat loss is dominated by convection at the cornea, and therefore accurate modelling of the choroidal blood flow is less important.

179 At higher frequencies the absorption is concentrated in the anterior part of the eye, and standing waves are not observed. Bernardi et al (1998) calculated SAR and temperature rise for several frequencies between 6 and 30 GHz. Comparing results using several geometric models of the eye and its surroundings, they found the maximum SAR significantly increased when scattering from the nose was considered. For a 10 W m^{-2} vertically polarised plane wave the maximum temperature rises were 0.04°C in the lens at 6 GHz and 0.06°C in the cornea at 18 GHz. It is suggested that the use of spectacles could in some circumstances increase the average SAR by as much as 30%. The authors concluded that for this frequency range a 10 W m^{-2} 'standard' provides a sufficient safety factor, but if the power density were scaled to reach the ICNIRP basic restriction for general public exposure (2 W kg^{-1} averaged over 10 g) the lens temperature could rise by 0.6°C. However, this value was obtained at 18 and 30 GHz, frequencies at which the power density, not the SAR, is restricted by ICNIRP guidelines.

Heating of the head

180 Recent concerns over possible effects of mobile phone usage have motivated research into microwave exposure of the whole head. These models address not only thermal effects in the eye, but also sensitive locations in the brain, such as the hypothalamus, which is the central temperature controller for the body. Most of the studies concentrate on the calculation of the temperature rise due to direct absorption of electromagnetic energy in the head. It is important to note that when using a mobile phone this is only one of the mechanisms that serve to raise the brain temperature; heat is also generated within the phone and conducted to the head, and pressing the phone to the ear inhibits heat loss from the skin. Most of these studies utilised FDTD computations of SAR followed by a finite-difference solution of the bioheat equation.

181 Fujiwara et al (1999) computed temperature rises in the head generated by plane waves incident in the antero–posterior (AP) direction at 1.5 GHz. Their results are quoted for an incident power density of 50 W m^{-2}. Since temperature dependence of the tissue properties was neglected, the results for 10 W m^{-2} exposure can simply be

rescaled in order to compare with those of other authors. When this is done the peak temperature rises are 0.07°C in the eye and muscle, 0.034°C in the brain, and 0.00052°C in the hypothalamus. This last figure is too small to trigger thermoregulatory responses for incident power densities of 10, 50 or even 100 W m^{-2}, the reference levels most often used in international standards. The predicted time evolution of temperature in each organ is consistent with the hypothesis that all time constants are greater than 6 minutes.

182 Yano et al (2001) followed up the above study, examining the sensitivity of temperature rise to blood flow in the brain and comparing results for adult and infant head models. Their infant head model had a depth of 10.5 cm in the AP direction, compared with 19.25 cm for the adult. For the infant model a distinct localised temperature rise was observed. Peak values of SAR and temperature were greater in the adult, but values averaged over the whole brain were greater in the infant because of this localised increase. The average temperature rise in the infant brain was three times that in the adult. The maximum temperature rise for a power density of 10 W m^{-2}, was 0.07°C for the adult (in the eye) and 0.055°C for the child (in muscle). These corresponded to 1 g averaged SAR values of 0.52 and 0.61 W kg^{-1}, respectively. It should be noted that these computations were done with incident plane waves; highly localised effects are usually much less pronounced when near-field sources are used.

183 Wang and Fujiwara (1999) calculated temperature rises in the head induced by a more realistic model of a mobile phone, namely a quarter-wavelength monopole antenna on a metal box. They considered two frequencies, 900 MHz and 1.5 GHz. When antenna power is scaled to 1 W, the predicted maximum temperature rises in the brain are 0.09–0.15°C at 900 MHz, and 0.17–0.27°C at 1.5 GHz. In each case the lower value was obtained with the handset just touching the ear and the higher with the handset pressed more closely to the head. The corresponding peak 1 g averaged SAR values were 1.48–2.82 W kg^{-1} at 900 MHz, and 2.15–4.85 W kg^{-1} at 1.5 GHz. The corresponding peak 10 g averaged SAR values were 1.1–2.05 W kg^{-1} at 900 MHz, and 1.41–3.3 W kg^{-1} at 1.5 GHz. At the IEEE SAR exposure limit for the uncontrolled environment (1.6 W kg^{-1} averaged over 1 g), the maximum temperature rise in the brain was 0.06°C, and at the ICNIRP basic restriction (2 W kg^{-1} averaged over 10 g) it was 0.11°C.

184 Wainwright (2000) computed temperature rises in the brain using a finite-element method, using SAR profiles previously calculated by FDTD (Dimbylow and Mann, 1994). The source model was again a monopole on a metal box. Both horizontal and vertical antenna orientations were considered for a phone at the side of the head, as well as an antenna position in front of the eye. Temperature rises in the brain for a 1 W antenna were calculated between 0.14 and 0.4°C. For exposure at 1 W kg^{-1} (averaged over 10 g) the corresponding temperature rises were between 0.109 and 0.164°C. During subsequent development, the geometry of the model has been refined. The temperature results have been reanalysed and the highest value calculated is 0.122°C (Wainwright, unpublished data).

185 Van Leeuwen et al (1999) introduced a detailed description of individual blood vessels in the side of the head adjacent to a closely spaced 915 MHz dipole antenna simulating a mobile phone. The maximum temperature rise in the brain was predicted

to be about 0.11°C for a 0.25 W antenna output power, corresponding to an SAR of 0.91 W kg^{-1} averaged over a 10 g cube, or 1.66 W kg^{-1} averaged over an arbitrary 10 g region. They also performed calculations using the Pennes bioheat equation and found results of the same order. Limited experimental validation was done by measuring skin surface temperatures using infrared thermography.

186 Gandhi et al (2001b) calculated temperature rises in the head taking into account the effect of SAR together with conduction from a warm (39°C) mobile phone and reduction of heat loss by a phone held to the ear. Frequencies of 835 and 1900 MHz were considered. For an input power of 10 W kg^{-1}, they predicted temperature rises of 0.5°C in the brain. Temperature rises in the pinna were found to be around 4.5°C due to conduction and suppression of convection.

187 Bernardi et al (2000) investigated temperature rises in the head with four different types of antenna on a mobile phone. Their results suggested a maximum temperature increase in the external part of the brain from 0.10–0.16°C for every 1 W kg^{-1} of SAR averaged over 1 g.

188 Hirata and Shiozawa (2003) have calculated the SAR and resultant temperature rise for a large ensemble of different exposure conditions. The exposure conditions were characterised by multiple parameters: the phone was pressed against the ear, flattening it against the head, or not; the frequency was varied over five values between 900 MHz and 2.45 GHz; polarization was horizontal or vertical; 18 different antenna feed points were used on a dipole antenna. Monopole and helical antennas were also examined. By statistical analysis of these results (a total of 660 cases in all), regression lines were established relating temperature rise to 1 g and 10 g SAR averages. The authors concluded that the maximum temperature rise in the whole head was better correlated with the 10 g average, whereas the maximum temperature rise in the brain was better correlated with the 1 g average. At 2 W kg^{-1} per 10 g of tissue (the ICNIRP general public basic restriction) the authors predicted for their worst-case exposure scenario a maximum temperature rise of 0.25°C in the brain.

189 In summary, temperature rises generated in the brain per unit SAR have been calculated for exposures at mobile phone frequencies. Predictions range from about 0.05 to 0.12°C per W kg^{-1}. Little work has been done on thermal dosimetry in general at other frequencies. However, at frequencies above about 10 GHz the field penetration depth is reduced to a few millimetres or less, and significant absorption in the brain is not expected. At lower frequencies the absorption pattern in the head becomes more uniform, and anomalously high localised SAR values are unlikely.

190 For the above reasons, and because of the importance of mobile telephony as a source of exposure, the studies carried out at 800-1900 MHz provide the most important data when recommending restrictions on SAR to avoid thermal effects in the brain.

Microwave auditory effect

191 Under exposure to pulsed microwaves, auditory sensations may be produced (Guy et al, 1975; Elder and Chou, 2003). It is now widely accepted that thermoelastic expansion is the most likely mechanism for this phenomenon.

192 Watanabe et al (2000) used an FDTD method to compute thermoelastic waves generated by a 915 MHz plane-wave pulse, incident on the back of the head. Dominant

frequency components at 7–9 kHz correspond to resonant frequencies of pressure waves in the head. A variety of pulse durations were investigated, from 1 to 180 μs. The relative loudness of the acoustic signal was found to have several maxima as a function of pulse duration, notably at 50 μs, which is a half-cycle of the resonant frequency. The threshold power density for audition was predicted by calculating the power density that would generate the same peak pressure as the threshold of bone conduction hearing. The predicted threshold, 3 kW m^{-2}, is near to that which has been measured experimentally.

Whole-body exposure and heat stress

193 In view of the large number of unknown parameters in any whole-body thermal model of man, the best guide to the resulting rise in core temperature is still experimental. Several simplified models have been used; however, to validate the parameters related to thermoregulation it is necessary to refer to volunteer experiments in situations where significant thermoregulatory adjustments are produced, for example, in MRI exposures.

194 For example, using a simple two-compartment lumped parameter model, Adair and Berglund (1986) have calculated that an indefinitely long exposure could be carried out at a whole-body SAR of 5 W kg^{-1} without raising core temperature by more than 0.6°C, while 3 W kg^{-1} would not raise core temperature by more than 0.2°C. The standard parameters of this model are derived from measurement of healthy volunteers; considerable variation can be expected among individuals, particularly those with compromised thermoregulatory systems. As this model was applied to MRI procedures, it was assumed that the subject wore light clothing (pyjamas). At SAR values greater than 5 W kg^{-1} skin blood flow was predicted to increase over 25 minutes to its maximal rate of 90 litres per hour per square metre. This response requires increases in heart rate and total cardiac output, which could be harmful to subjects with impaired cardiovascular function. These results are reasonably consistent with the available experimental data (see paragraphs 26–28).

Averaging mass

195 In most guidelines for the limitation of SAR, it is not the spatial peak SAR but some suitable average that is constrained. The size of the region over which averaging should be done is a matter of debate. The averaging mass serves two purposes: firstly, it provides a definition of SAR that is robust and not overly sensitive to slight changes in exposure setup; secondly, it takes into account the spatial dispersion of the deposited energy which is provided by heat transfer mechanisms.

196 It is not possible to constrain the maximum temperature rise in the body by limiting any averaged measure of SAR. A sufficiently concentrated heat source can produce arbitrarily high temperatures at a point (eg an idealised point source would produce a singular temperature distribution).

197 However, an acceptable averaging mass can be deduced by considering the characteristic length scales of heat transfer and expected inhomogeneities in the SAR distribution. The scale of SAR inhomogeneities is itself determined by several factors, including the penetration depth of the field (which depends on frequency) and the scale of those anatomical features that may cause localised increases in absorption. The size of the averaging region should be no larger than the smallest of these length scales.

198 The Pennes bioheat equation contains a natural length scale

$$L = \sqrt{\frac{k}{\rho_b c_b \rho \omega}} \tag{4}$$

In one-dimensional heat flow this is the distance over which conducted heat flux is reduced by a factor 1/e due to the heat sink. Here ρ is the density, c the specific heat capacity and k the thermal conductivity of the tissue, the subscript 'b' indicates the corresponding parameters for blood, and ω is the blood perfusion rate. In normally perfused muscle this is about 14 mm; in more highly perfused brain tissue it is about 4 mm.

199 A long, thin region or a widely spaced set of disconnected regions may be discounted since such a region will lose heat by conduction much faster than a compact region, such as a sphere or a cube. Since any disconnected region can be made connected by the addition of arbitrarily thin bridges, merely specifying that the region should be contiguous does not exclude these thermally insignificant regions from the average. Some dosimetric studies have cited the maximum SAR averages over any 10 g cube; this quantity is probably a better predictor of temperature rise and thermal effects. Studies such as that of van Leeuwen et al (1999) have suggested that in some circumstances the average over an arbitrary contiguous region may be 50–100% greater than that over a cubic region. This should be considered when defining a procedure for measuring or calculating SAR in the future development of exposure guidelines.

200 Bearing in mind the above points, the averaging regions should have a compact shape, such as a sphere or a cube. It is judged that the averaging mass for exposure of the head should be no greater than 10 g, since this is approximately the size of the eyeball and localised increases in absorption can certainly be created on this scale (see paragraphs 174–179). At frequencies around 4 GHz, the penetration depth is around a centimetre and decreases to around a millimetre at 10 GHz. Above this frequency, the temperature rise is well correlated with the incident power density.

201 The choice of averaging mass is clearly most important for highly localised exposure. At the other extreme, a uniform SAR distribution gives the same average whatever mass is used. Some authors have cited results both in terms of 1 g (IEEE, 1992) and 10 g (ICNIRP, 1998) averaging masses. It is reasonable to expect the greatest differences will be for situations of near-field exposure to an antenna such as a mobile phone. However, most authors (eg van Leeuwen et al, 1999; Wang and Fujiwara, 1999) find no more than a factor of two between the SAR values calculated in these two ways.

Dosimetric uncertainties

202 Sources of uncertainty in EMF calculations include the reliability of numerical methods, different individual anatomies and postures, resolution and variation in dielectric parameters.

203 Dimbylow (2002) showed that the whole-body averaged SAR is a robust quantity with respect to model resolution and a comparison with other fine resolution calculations showed an agreement within 10%.

204 The thermal and electrical properties of tissue have been studied extensively using samples obtained from a variety of animal species. Factors that lead to uncertainty in measured values of these properties include temperature, degree of hydration, time since death, inter-species variations and age.

205 Gajsek et al (2001) investigated the dependence of SAR values from 70 to 2000 MHz on tissue dielectric properties using the 3 mm version of the Brooks digital anatomical man using the Gabriel et al parameters as the baseline (Gabriel, 1996; Gabriel et al, 1996a–c). Gajsek et al found that when they changed the conductivity and relative permittivity of all tissues either by 0.5 times or by 2.0 times the Gabriel (1996) values, the whole-body SAR remained within a 20% bound. In contrast, the localised SAR in organs was substantially influenced by variability in dielectric parameters. Changing the values of muscle by a factor of two resulted in local SAR ratio changes by a factor of two in almost 50% of tissue types. They concluded that there is no universal approach to predicting the relative changes in localised SAR values from variations in dielectric parameters and each case had to be treated individually.

206 A major source of variation between reported results, especially for near-field sources such as mobile phone handsets, is the difference between geometries used by the authors. For example, the SAR and hence temperature rise in the brain is critically dependent on the distance between the antenna and the brain. The brain temperature rise for a given SAR depends on exactly where the energy is deposited, and may vary by a factor of between two and five.

207 Computational models of heating are critically dependent on the use of accurate values of the blood flow rate (or perfusion) in various tissues and organs. In many cases these have not been adequately determined for humans. For example, models of heat transfer in the eye, which have been validated by experimental work on rabbits or non-human primates, should be applied to people only with caution.

208 Adverse effects due to heating are very dependent on the efficiency of the thermo-regulatory system. This varies with age and health status (see paragraphs 29–35). People with impaired thermoregulatory or cardiovascular function should be considered in the development of exposure guidelines.

209 The relationship between temperature rise and SAR, as well as the SAR for a given external field, may be dependent on age. It is known that the dielectric properties of rat tissues vary with age (Peyman et al, 2001), and it has been suggested that a similar trend in human tissues may lead to increased vulnerability of children to RF EMFs from mobile phones and base stations (IEGMP, 2000). It is to be expected that changes in the composition of tissues, particularly their level of hydration, will also have consequences for their thermal properties. Other significant differences in thermal physiology between adults and children (see paragraph 39) should also be taken into consideration, as should differences in body morphology. The net effect of all these changes cannot easily be predicted; it is not clear whether their overall effect is to increase or decrease the effects of exposure in children. Further research is needed in this area.

Summary

210 Computational dosimetry provides a link between external non-perturbed EMFs and the fields induced within the body. This gives guidance to the choice of reference levels in relation to basic restrictions. Exposure guidelines provide basic restrictions on

SAR between 100 kHz and 10 GHz to prevent whole-body heat stress and excessive localised tissue heating. The usual approach to deriving reference levels based on SAR is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic models of the body. Computational techniques may also be used to relate SAR to temperature rises within the body, thereby helping to indicate basic restrictions on SAR which will avoid adverse thermal effects.

211 The Finite-Difference Time-Domain (FDTD) method is well suited for application to voxel phantoms. The method follows the time evolution of the propagation, reflection and absorption of electromagnetic waves in a domain comprising the target and surrounding space. The domain is divided into a three-dimensional lattice of cells that are assigned discrete electrical properties.

212 The FDTD method has been applied to calculate whole-body averaged SAR for adults and children from frequencies ranging from 10 MHz up to 3 GHz. The whole-body resonance of maximum energy absorption occurs when the height of the body is approximately $\lambda/2$, where λ is the wavelength in air. When the phantom is grounded, the reflection in the ground plane halves the resonant frequency. High, localised SAR values can occur in the wrists and ankles, which have a narrow cross-section with little high conductivity muscle. Recently there has been interest in the deposition of energy in the head from mobile phones. There are contradictory reports as to whether there are significant differences in the absorption of SAR in the heads of adults and children.

213 The most appropriate computational technique for thermal modelling depends on the exposure conditions. In circumstances where the whole body is exposed at a level which causes elevation of the core temperature and consequent thermoregulatory responses, coarsely segmented models of the whole body have been used. At frequencies greater than about 10 GHz, absorption of electromagnetic energy takes place mostly in the skin and other superficial tissues. When the penetration depth of the field is small compared with the radius of curvature of the body surface, one-dimensional models of electromagnetic propagation and heat transfer may be used. Most theoretical studies of localised or regional heating use some variant of the Pennes bioheat equation. Recent concerns over possible effects of mobile phone usage have motivated research into microwave exposure of the whole head. Most of these studies utilised FDTD computations of SAR followed by a finite-difference solution of the bioheat equation. From the several recent independent computational studies of mobile phone exposure, it seems that a localised SAR of 1 W kg^{-1} (averaged over 10 g) should not cause an increase in brain temperature of more than about 0.12°C.

214 The localised SAR averaging mass serves two purposes: firstly, it provides a definition of SAR which is robust and not overly sensitive to slight changes in exposure setup; secondly, it takes into account the spatial dispersion of the deposited energy which is provided by heat transfer mechanisms. An acceptable averaging mass can be deduced by considering the characteristic length scales of heat transfer and expected inhomogeneities in the SAR distribution. It is judged that the averaging mass for exposure of the head should be no greater than 10 g.

215 Sources of uncertainty in calculations include the reliability of numerical methods, different anatomies and postures, resolution and variation in dielectric and thermal parameters.

The approach to deriving reference levels for RF EMFs is to solve Maxwell's equations numerically, in fine resolution, anatomically realistic voxel models of the body.

The whole-body averaged SAR is a robust quantity with respect to model resolution. Comparisons between different voxel model calculations showed an agreement within 10%. Even changes of the conductivity and relative permittivity of all tissues, either by 0.5 times or by 2.0 times, still provide whole-body SAR values within a 20% bound.

The whole-body resonance of maximum energy absorption occurs, for uniform exposure under isolated conditions, when the height of the body is approximately half a wavelength in air. When the body is uniformly exposed under grounded conditions, the reflection in the ground plane halves the resonant frequency.

Children would generally have higher resonant frequencies than adults due to their reduced heights and so it is important to include them in reference level calculations.

For exposure to RF EMFs from mobile phones, there are conflicting reports as to whether there is a significant increase in the SAR absorbed in the head, and particularly in the brain, for children compared with adults.

There is an absence of SAR evaluations in pregnant women and related heating in the embryo and fetus.

From the several recent independent computational studies of mobile phone exposure, it seems that a localised SAR of 1 W kg^{-1} (averaged over 10 g) should not cause an increase in brain temperature of more than about 0.12°C.

Other studies have addressed plane-wave exposure of the eye at frequencies up to 30 GHz. At mobile phone frequencies, the computed temperature rises are similar to those found in the brain. At higher frequencies the temperature rise per unit SAR is greater. One study suggests that at 6 GHz, a localised SAR of 1 W kg^{-1} (averaged over the whole eye) produces a temperature rise of up to 0.25°C in the lens.

6 Scientific Uncertainty

1 This chapter addresses the interpretation of the scientific data and uncertainties in the context of identifying and assessing:

(a) effects that can be firmly concluded on scientific grounds as being caused by exposure to EMFs and where supporting scientific data are sufficient to be able to quantify appropriate restrictions on exposure,

(b) effects that have been associated with EMF exposure but where the scientific data are insufficient either to make a conclusive judgement on causality or to quantify appropriate restrictions on exposure.

2 The former of these two classes of adverse effects is relevant to recommending quantitative restrictions on exposure to EMFs. The latter is discussed in the context of the possible need for further precautionary measures.

3 NRPB concludes that there are scientific data indicating appropriate quantitative restrictions on exposure. These data derive from experimental studies related to effects of EMFs on the central nervous system at low frequencies and effects of heating on the body at higher frequencies. The nature of such effects and the mechanisms underlying them are reviewed in this document. Quantitative restrictions on exposure are derived from biological information on these effects.

4 Evidence of effects associated with EMF exposure, but where the scientific data are insufficient to make a judgement on causality or to quantify appropriate exposure restrictions, derives principally from epidemiological studies and from some experimental studies. The main, but not sole, subject of such studies has been cancer. These studies have been reviewed extensively by expert groups, including AGNIR, and are summarised and further reviewed in this document.

5 NRPB concludes that currently the results of these studies on EMFs and health, taken individually or as collectively reviewed by expert groups, are insufficient to establish causality of effect or derive quantitative restrictions on exposure to EMFs. This conclusion is in accord with the manner in which other expert bodies – for example, the International Commission on Non-Ionizing Radiation Protection (ICNIRP, 1998) – have developed EMF exposure guidelines. However, such studies, together with people's concerns, provide a basis for considering the possible need for further precautionary measures in addition to the application of quantitative restrictions on exposure to EMFs.

EMF HEALTH RISK ASSESSMENT

6 A health risk assessment for EMFs includes the determination of adverse effects on people's health as a result of exposure and, where possible, quantitative relationships between exposures and effects. In principle, such relationships may indicate the magnitude of the EMF exposure necessary to produce the effect where there is a threshold for the response and/or the probability of the effect occurring as a function of exposure. A health risk assessment addresses both possible short-term (immediate) and long-term (delayed) effects of exposure.

Evidence and uncertainties

7 The primary source of information for a health risk assessment is the published scientific evidence from epidemiological studies, human (volunteer) laboratory studies, and animal (bioassay) laboratory studies. For better understanding of the biochemical and biophysical mechanisms that may be involved, the results of *in vitro* studies should also be included. Thus, a necessary part of EMF health risk assessment is the examination of the scientific data in a holistic manner, bringing together and assessing the evidence from the life sciences. Physical dosimetry provides a link describing and quantifying fields external to the body (people or animals) in relation to fields induced inside the body.

8 All scientific investigations are subject to uncertainties, as is the interpretation of the studies relevant to judgements on likely adverse health effects. An example of the latter arises when the results of animal studies are extrapolated to possible effects in people because of inter-species and inter-strain differences that exist. Even the results from well-designed and well-conducted epidemiological and experimental studies have uncertainties that can be statistically quantified, but may not always be explained. Additionally, not all studies are well designed and executed and this should also be taken into account when assessing the available information. Thus, the risk assessment process should address these uncertainties in life science and dosimetry data.

EMF exposure guidelines and caution

9 NRPB considers that the exercise of caution based on knowledge and understanding of the sources of uncertainty in the scientific data is an intrinsic part of the EMF risk assessment process. The degree to which caution is applied in the interpretation of the scientific evidence is a matter of judgement and should be consistent. EMF exposure guidelines should ensure that general community protection is provided. In this document, the term 'precautionary' is reserved for measures that might be considered necessary in addition to quantitative restrictions on exposure derived from a 'cautious' interpretation of the science.

10 In recommending quantitative restrictions on exposure, NRPB has made judgements on the degree of uncertainty in the scientific data and how this indicates the choice of the restriction values. The basic restrictions recommended in this document for preventing direct adverse health effects of exposure to EMFs and other recommendations for limiting the occurrence of indirect effects (eg shock and burn) include such considerations and, overall, they reflect a cautious approach.

11 Judgements have been made concerning the need for exposure to be additionally restricted where increased susceptibility of groups of people is expected on scientific grounds, but where, because there is a lack of specific scientific data, the degree of susceptibility cannot currently be precisely determined. These judgements form the basis of recommendations for more restrictive exposure values for members of the public compared with those for workers.

12 Further, NRPB noted the advice provided by an ad hoc expert group on effects of weak electric fields (Appendix A) and by other experts at an ICNIRP/WHO workshop on weak electric field effects in the body (Appendix B; ICNIRP/WHO, 2003). As a result, it has concluded that internal electric field strength is the appropriate dosimetric quantity with which to express basic restrictions for low frequency electric and magnetic fields.

This judgement and other similar ones based on uncertainties and new scientific data are intended to stimulate scientific discussion towards the future development of EMF exposure guidelines.

International initiatives

13 WHO has launched an initiative aimed at achieving a harmonised international approach to the development of EMF exposure guidelines, a keystone of which is that they should be based on thorough reviews of the science. ICNIRP, NRPB and other national expert bodies concerned with the development of exposure guidelines have already adopted this approach.

14 The European Commission has urged the need for harmonisation of standards of protection within the European Union (EU). A Recommendation to EU Member States on the limitation of exposure of the general public to EMFs in the frequency range 0–300 GHz was passed on 12 July 1999 by the Council of the EU and published in the *Official Journal of the European Communities* (CEU, 1999). The UK supported the Recommendation.

15 In its preamble, the Recommendation states that 'measures with regard to electromagnetic fields should afford all Community citizens a high level of protection: provisions by Member States in this area should be based on a commonly agreed framework, so as to contribute to ensuring consistency of protection throughout the Community'. This message is reinforced in the Recommendation's explanatory material presented to the European Council by the Commission, where it states 'the existing variations and gaps in provisions and guidelines [in some Member States] contribute to a sense of confusion and insecurity felt by many Community citizens and undermines confidence in health protection authorities'.

16 The view of the European Council as to the importance of the ICNIRP guidelines, their scientific basis and the integrity of the ICNIRP approach is explicit:

> 'The Community framework, which draws on the large body of documentation that already exists, must be based on the best available scientific data and should comprise basic restrictions and reference levels on exposure to electromagnetic fields, recalling that only established effects have been used as the basis for recommended limitation of exposure; advice on this matter has been given by the International Commission on Non Ionising Radiation Protection and has been endorsed by the Commission's Scientific Steering Committee.'

17 NRPB advice on limiting exposure to EMFs has been developed from the reviews of the science, as detailed in this document, whilst noting the advantages of international harmonisation.

EMF EXPOSURES AND FURTHER PRECAUTION

18 The possible need for further precautionary measures with regard to EMF exposure, in addition to quantitative basic restrictions and reference levels, is considered here.

19 The relevance of adopting further precautionary measures for EMF exposure has been the subject of considerable debate internationally. An important and controversial aspect of that debate has been whether the Precautionary Principle is relevant in addressing possible risks to public health.

The Precautionary Principle

20 The Precautionary Principle has been succinctly described in plain English as 'better safe than sorry' and 'err on the side of caution' and in more political and technical terms as 'taking steps to avoid possible environmental or health damage, in the face of insufficient evidence' (Foster, 2002).

21 The basic principles for the Precautionary Principle were enunciated in the World Charter for Nature adopted by the United Nations General Assembly in 1982 (UN, 1982). It was subsequently incorporated in various international agreements on environmental protection, including the 1992 Rio Conference on the Environment and Development (EC, 2000). Principle 15 of the Rio Declaration states that 'in order to protect the environment, the precautionary approach shall be widely applied by States according to their capability. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation'.

22 It should be noted that all references in the Rio Declaration are to protection of *the environment* and there are no specific references to the health of communities or individuals. The 'Rio Principle' has subsequently become consolidated in international environmental law.

23 The World Health Organization offered clarification of the issue in the context of EMF exposure in 2000 in a 'backgrounder' document on cautionary policies for protection against EMFs – namely, that 'a principal requirement is that such policies be adopted only under the condition that scientific assessments of risk and science-based exposure limits should not be undermined by the adoption of arbitrary cautionary approaches' (WHO, 2000).

24 WHO defines health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' (WHO, 1946). Within this definition, effects on people's health due to their perception of the risk, whether real or imagined, should be addressed. Clearly death is the most severe adverse health outcome – but pain, disability, prolonged discomfort and other endpoints leading to a loss of quality of life should be considered as relevant.

25 Recently, WHO has produced a draft report on a 'Precautionary Framework for Public Health Protection' (WHO, 2003a)*. This document sets out 'an overarching approach encompassing procedures in managing human health risks that are either known or uncertain'. The document considers the principles of the health risk assessment process and does not specifically address EMFs or any other agents. Aspects of this are discussed in paragraphs 38–48 below.

European dimension

26 The European Commission (EC) has taken a leading role in fostering discussion on the use of the Precautionary Principle, mainly through the publication of a Communication from the Commission on the Precautionary Principle (EC, 2000). This document sets out the EC approach to using the Precautionary Principle: establishing guidelines for applying it; building a common understanding of how to assess, appraise,

* It should be noted that this document is currently in the form of a draft for comment and may be subject to change. It therefore does not necessarily represent WHO policy.

manage and communicate risks that science is not yet able to evaluate fully; and to avoid unwarranted recourse to the Precautionary Principle as a disguised form of protectionism. The stated aim of the document is not to be prescriptive but rather to be used as general guidance and as an input to the ongoing debate. However, it should be viewed in the context of a resolution adopted by the European Council on 13 April 1999 urging the EC 'to be in future even more determined to be guided by the Precautionary Principle in preparing proposals for legislation and in its other consumer-related activities and develop as priority clear and effective guidelines for application of this principle' (EC, 2000). The EC-published Precautionary Principle document is part of the EC response to this resolution.

27 There is an explicit (legal) reference to the Precautionary Principle in the environment title of the EC Treaty (of Rome) (EC, 2000). Here, the reference of application is again to the environment but the EC states that this cannot be interpreted as applying *only* to the environment. The EC sets out its case for this view on the basis of examples of case law and policy and arrives at the following conclusion. 'Although the Precautionary Principle is not explicitly mentioned in the Treaty except in the environment field, its scope is far wider and covers those specific circumstances where scientific evidence is insufficient, inconclusive or uncertain and there are indications through preliminary objective scientific evaluation that there are reasonable grounds for concern that the potential dangerous effects on the environment, human, animal or plant health may be inconsistent with the chosen level of protection.'

28 The EC clarified the circumstances of the use of the Precautionary Principle and the difference between 'risk' and 'effect' as 'Recourse to the Precautionary Principle presupposes: (i) identification of potentially negative effects resulting from a phenomenon, product or procedure, and (ii) a scientific evaluation of the risk that because of the insufficiency of data, their inconclusive or imprecise nature, makes it impossible to determine with sufficient certainty the risk in question' (EC, 2000).

29 In December 2000 at the Nice Summit, heads of government endorsed a General Affairs Council resolution on the Precautionary Principle (CO-SUR, 2002). This provided as follows.

> 'Use must be made of the Precautionary Principle where the possibility of harmful effects on health or the environment has been identified and preliminary scientific evaluation proves inconclusive for assessing the level of risk.
>
> 'The scientific assessment of the risk must proceed logically in an effort to achieve hazard identification, hazard characterisation, and appraisal of exposure and risk characterisation.
>
> 'Risk management measures must be taken by the public authorities responsible on the basis of a political appraisal of the desired level of protection.
>
> 'All stages must be conducted in a transparent manner, civil society must be involved and special attention must be paid to consulting all interested parties as early as possible.
>
> 'Measures must observe the principle of proportionality, taking account of short-term and long-term risks; must not be applied in a way resulting in arbitrary or unwarranted discrimination; and should be consistent with measures already adopted in similar circumstances or following similar approaches.

> 'Measures adopted presuppose examination of the benefits and costs of action and inaction, and the examination must take account of social and environmental costs and of the public acceptability of the different options possible.
>
> 'Decisions taken in accordance with the Precautionary Principle should be reviewed in the light of developments in scientific knowledge.'

UK dimension

30 Risk management is a stated priority of the UK government and a strategy has been published aiming towards it being an integral part of the business of good government. In the foreword to a Strategy Unit Report published in November 2002, the Prime Minister wrote 'It will rarely be possible for governments to eliminate risks entirely. All life involves some risk, and innovation brings risks as well as reward – so the priority must be to manage risks better' (CO-SUR, 2002).

31 This report effectively sets out the manner in which the UK government should think about risk and practical steps for managing it better.

32 Specifically on the 'Precautionary Principle', the report provides a definition and guidance on its use as follows.

> 'The Precautionary Principle provides a framework for action by governments where there is a threat of serious or irreversible harm even where there is scientific uncertainty about the nature and extent of the risk. The UK, along with other developed countries, is committed to using the Precautionary Principle.
>
> 'The Principle is based on Principle 15 of the 1992 Rio Declaration, which states: 'where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation'.
>
> 'There is no universally accepted definition of the Precautionary Principle. Since Rio, it has been included in a number of international agreements in a variety of formulations that reflect the substantive context and the negotiating circumstances of the individual agreements.'

33 These observations broadly align with the views promulgated by the EC, as summarised in paragraphs 26–29.

34 The UK government commissioned an Inter-departmental Liaison Group on Risk Assessment (ILGRA) to develop guidance on a more consistent approach to application of the Precautionary Principle across government (ILGRA, 2002). The key points of ILGRA guidance are summarised below.

35 ILGRA recommends that the Precautionary Principle should be invoked when:

> 'There is good reason to believe that harmful effects may occur to human, animal or plant health or to the environment.
>
> 'The level of scientific uncertainty about the consequences or likelihood of the risk is such that the best available scientific advice cannot assess the risk with sufficient confidence to inform decision-making.'

36 ILGRA guidance also makes the following recommendations.

> 'The Precautionary Principle should be distinguished from other drivers that require caution such as society's view on the extent of protection afforded to children or others considered to be vulnerable, or the wish to ensure that conventional risk assessment techniques deliberately overestimate rather than underestimate risk.

'Action in response to the Precautionary Principle should accord with the principles of good regulation, ie be proportionate, consistent, targeted, transparent and accountable.

'Applying the Precautionary Principle is essentially a matter of making assumptions about consequences and likelihoods to establish credible scenarios, and then using standard procedures of risk assessment and management to inform decisions on how to address the hazard or threat.

'Decision-making should bring together all relevant social, political, economic and ethical factors in selecting an appropriate risk management option.

'Invoking the Precautionary Principle shifts the burden of proof in demonstrating presence of risk or degree of safety towards the hazard creator. The presumption should be that the hazard creator should provide, as a minimum, the information needed for decision-making.

'Decisions reached by invoking and applying the Precautionary Principle should be actively reviewed, and revisited when further information that reduces uncertainty becomes available.'

37 NRPB notes particularly the comments by ILGRA on 'the wish to ensure that conventional risk assessment techniques deliberately overestimate rather than underestimate risk'. It is the view of NRPB that EMF health risk assessment and derivation of quantitative exposure restrictions should generally lean towards the side of caution in reaching a judgement on quantitative levels of exposure restriction.

PRECAUTIONARY MEASURES

WHO precautionary framework

38 There is no scientific consensus that exposures to EMFs at levels below currently accepted UK or international exposure restrictions cause cancer or any other disease. However, it is the view of NRPB that the totality of the scientific data and uncertainty in knowledge and/or other relevant factors indicate that consideration should be given as to whether further precautionary measures are needed.

39 A workshop jointly organised by WHO, the EC and the US National Institute for Environmental Health Sciences (NIEHS) was held in Luxembourg in February 2003 that specifically addressed this topic. Subsequent to the workshop, WHO has produced a draft document for comment on a Precautionary Framework for Public Health Protection (WHO, 2003a) *.

40 NRPB welcomes this initiative to clarify this important issue and the following paragraphs summarise some of the key points addressed in the WHO draft document.

41 WHO introduces a new term, 'the WHO Precautionary Principle for Public Health', which it defines as 'a concept that allows flexible approaches to identifying and managing possible adverse consequences to human health even when it has not been established that an activity or exposure constitutes harm to health'.

* It should be noted that this document is currently in the form of a draft for comment and may be subject to change. It therefore does not necessarily represent WHO policy.

42 WHO also describes a 'WHO precautionary framework for public health protection', which is 'an overarching approach encompassing procedures in managing human health risks that are either known or uncertain'.

43 WHO notes that current risk management systems focus on what is known and therefore science plays a key role. It emphasises that similarly science plays a key role in its proposed precautionary framework for public health protection and that its use is not at odds with scientific understanding.

44 As expressed in the draft document, the view of WHO is that current risk management has the following aspects.

> 'Overall evaluation is based on the weight-of-evidence. The science must be rigorous, appropriately multidisciplinary, published in a peer-reviewed journal and relevant to risk assessment.
>
> 'Uncertainties can exist at every level of risk assessment: the existence of a hazard, the magnitude of exposure, and the relationship of dose to disease incidence or severity. Uncertainties and assumptions necessary for the proper assessment of risk must be identified and clearly stated.
>
> 'When evidence does not meet generally accepted conventional scientific standards, science-informed assumptions or extrapolations are used.'

45 WHO notes that its precautionary framework 'operates from a broader knowledge base and attempts to illuminate what is not known in addition to what is uncertain. Here too science plays a key role. The evaluation of both boundaries and gaps in current knowledge can and should be determined with scientific input.

> 'A description of when key evidence (eg epidemiological or toxicological studies) is missing or inadequate is especially important.
>
> 'Failure to demonstrate an adverse health effect in a limited timeframe does not rule out the possibility that it will occur sometime in the future.
>
> 'Failure to demonstrate an adverse health effect does not rule out its possible existence since the test system may be too insensitive to detect an effect.
>
> 'Identifying what is not known does not mean that actions would have to be implemented for any and all activities and exposures.'

46 NRPB notes that WHO states its precautionary framework is not a basis for extending or replacing science-based guidelines. Explicitly, WHO states that 'international guidelines limiting human exposures are supported by health effects research results that are consistent, reproducible, confirmed by different laboratories and clearly identify when exposure to physical, biological or chemical agents is thought to be harmful to humans. In addition, exposure limits generally incorporate safety factors that allow for uncertainty in any identified thresholds for established effects. Such approaches remain essential within the WHO precautionary framework'.

47 The approach taken by NRPB in developing its advice on limiting exposure to EMFs is consistent with these concepts.

48 NRPB generally supports the concepts in the WHO draft document and considers that, with further development, such a framework can be an effective tool for considering the possible need for precautionary measures in relation to health in general and EMF exposure in particular.

Application to EMFs

Power frequency fields

49 In the context of possible adverse health effects from EMFs, the conclusions of published expert scientific reviews have identified only one reasonably consistent epidemiological finding of an adverse health outcome associated with exposure to EMFs at levels lower than exposure guidelines: that is an apparent increased risk of childhood leukaemia with time-weighted average exposure to power frequency magnetic fields above 0.4 μT. It is the view of NRPB that the epidemiological evidence that prolonged exposure to power frequency magnetic fields above 0.4 μT is associated with a small absolute raised risk of leukaemia in children (an approximate doubling of the relative risk) is, at present, an observation for which there is no sound scientific explanation. This is consistent with the conclusions of the Advisory Group on Non-ionising Radiation (AGNIR, 2001a). There is no clear evidence of a carcinogenic effect of extremely low frequency EMFs in adults, and no plausible biological explanation of the association from experiments with animals or from cellular and molecular studies. Alternative explanations for this association are possible; for example, potential bias in the selection of control children with whom leukaemia cases were compared in some studies, and chance variations resulting from small numbers of individuals affected. Thus any judgements developed on the assumption that the association is causal would be subject to a very high level of uncertainty.

50 The International Agency for Research on Cancer (IARC) has classified power frequency magnetic fields as a possible carcinogen (IARC, 2002).

51 Public concern about possible risks from exposure to power frequency magnetic fields is also important and must be addressed. NRPB is aware of, and sympathetic to, the concerns about EMFs and health expressed by members of the public through both the individual and media enquiries to which it responds. NRPB welcomed the positive response from members of the public and others who participated in an open discussion meeting on power lines that it organised at the National Exhibition Centre, Birmingham, in December 2002.

52 Because of the uncertainty cited above, and in the absence of a 'dose–response' relationship, NRPB has concluded that the data concerning childhood leukaemia cannot be used to derive quantitative guidance on restricting exposure.

53 NRPB concludes that it is important to consider the possible need for precautionary measures with respect to exposure of children to power frequency magnetic fields.

Radiofrequency fields

54 AGNIR examined possible health effects of exposure to radiofrequency (RF) fields (AGNIR, 2003), with an emphasis on studies conducted since the review by the Independent Expert Group on Mobile Phones in 2000 (IEGMP, 2000). AGNIR noted that there are many sources of RF – at work, at home, and in the environment – but recent emphasis in health-related studies has been on mobile phones and broadcasting masts.

55 AGNIR also noted that studies reviewed by IEGMP suggested possible cognitive effects of exposure to RF fields from mobile phones, and possible effects of pulse-modulated RF fields on calcium efflux from the nervous system. AGNIR concluded that the overall evidence on cognitive effects remained inconclusive, while the suggestions of effects on calcium efflux had not been supported by more recent, better conducted

studies. The biological evidence suggested that RF fields do not cause mutation or initiate or promote tumour formation, and the epidemiological data overall do not suggest causal associations between exposures to RF fields, in particular from mobile phone use, and the risk of cancer. AGNIR noted that exposure levels from living near to mobile phone base stations are extremely low, and concluded that the overall evidence indicates that they are unlikely to pose a risk to health. With respect to possible risks to children's health, AGNIR noted that little has been published specifically on childhood exposures to RF fields and no new substantial studies had been published since the IEGMP report.

56 Overall, AGNIR concluded that, in aggregate, the research published since the IEGMP report does not give cause for concern and that the weight of evidence now available does not suggest that there are adverse health effects from exposures to RF fields below guideline levels. In reaching these conclusions, AGNIR noted that the published research on RF exposures and health has limitations and mobile phones have only been in widespread use for a relatively short time. The possibility therefore remains open that there could be health effects from exposure to RF fields below guideline levels; hence continued research is needed.

57 From its own review and the advice from AGNIR above, NRPB concludes that the scientific evidence for RF fields causing adverse health effects at levels to which the general public are normally exposed is much weaker than that for power frequency magnetic fields. It also notes there is a great deal of ongoing scientific research on RF fields, in particular mobile telephony, and health. There is a need to constantly monitor the results of this research.

7 Conclusions and Recommendations

In establishing quantitative restrictions on exposure to electromagnetic fields (EMFs), a range of values is possible; particularly when taking account of uncertainties in the responses of different groups of individuals in the general population. The review of current scientific knowledge by NRPB staff, the adoption of a cautious approach to the interpretation of these data, and a recognition of the benefits of international harmonisation, combine in a recommendation to adopt the ICNIRP exposure guidelines for occupational and general public exposure to EMFs between 0 and 300 GHz.

INTRODUCTION

1 Scientific evidence related to biological effects of electromagnetic fields (EMFs) and possible consequential adverse effects on human health has been reviewed in this document. In evaluating the basis for providing guidance on limiting exposure and possible risks from exposure to EMFs, consideration has been given to uncertainties in scientific data and a cautious approach has been adopted in their interpretation.

2 The review has covered epidemiological studies as well as experimental biology, volunteer studies and dosimetry. These play important individual and collective roles in identifying possible adverse effects on health and in providing information on the need for, and appropriate levels of, protection.

3 Based on the review, this chapter summarises the NRPB conclusions and recommendations including:

(a) the basis for providing quantitative restrictions on exposure of people to EMFs,
(b) basic restrictions on exposure to EMFs to avoid direct effects,
(c) advice on limiting possible indirect effects of exposure (shock and burn),
(d) reference levels, which are measurable quantities for assessing compliance with basic restrictions or for assessing the possibility of shock and burn,
(e) the possible need for further precautionary measures in relation to EMF exposure and health.

4 The recommendations are not concerned with exposures of patients carried out under medical supervision or with possible electrical interference with implantable medical devices such as pacemakers. They do not address detailed aspects of applying the guidelines to specific exposure situations.

5 A number of recommendations are made which are specifically aimed at developing guidance through research in key areas where continuing uncertainty limits the rigour with which appropriate restrictions on exposure can be formulated.

6 NRPB is committed to ongoing monitoring of the results of scientific studies on EMFs and health and to revising its advice when appropriate.

GENERAL CONCLUSIONS ON THE SCIENCE

7 NRPB concludes that there are scientific data indicating the need for appropriate quantitative restrictions on exposure. These data derive from experimental studies related to effects of EMFs on the central nervous system (CNS) and effects of heating on the body. The nature of such effects and the mechanisms underlying them have been reviewed in this document. The quantitative restrictions on exposure and recommendations for further investigation, where relevant, are derived from data on these effects.

8 Evidence of other possible effects associated with EMF exposure derives principally from epidemiological studies and from some experimental studies. The main, but not sole, subject of such studies has been cancer. These studies have been reviewed extensively by expert groups, including AGNIR, and are summarised in this document. It is concluded that currently the results of these studies on EMFs and health, taken individually or as collectively reviewed by expert groups, are insufficient either to make a conclusive judgement on causality or to quantify appropriate exposure restrictions. This conclusion is in accord with the manner in which other expert bodies – for example, ICNIRP (1998) – have developed EMF exposure guidelines.

9 However, such studies taken together with people's concerns provide a basis for considering the possible need for further precautionary measures in addition to the application of quantitative restrictions on exposure to EMFs.

EXPOSURE CIRCUMSTANCES

10 The basic restrictions on exposure to EMFs recommended in this document distinguish between occupational and general public exposure situations. This is a departure from previous NRPB advice and is supported by this review of the science.

11 NRPB notes exposure in occupational situations will generally be to healthy adults working under controlled conditions. These conditions include the opportunity to apply engineering and administrative measures and, where necessary and practical, provide personal protection.

12 NRPB also notes the general public includes people of all ages and widely varying health status, and exposure is likely to occur under uncontrolled conditions.

STATIC ELECTRIC AND MAGNETIC FIELDS

13 The perception threshold for static electric fields is around 20 kV m^{-1}, and annoying sensations can be induced above about 25 kV m^{-1}. Painful spark discharges can arise when a person who is well insulated from ground touches a grounded object, or when a grounded person touches a conductive object that is well insulated from ground; however, threshold static electric field values will vary depending on the degree of insulation and other factors.

14 Where static electric fields cause annoyance, or pain from electrostatic discharge, it is important to reduce the possibility of occurrence of these effects.

15 Vertigo, nausea, a metallic taste and phosphenes can be induced during movement in static magnetic fields larger than about 2 T; in addition, flow potentials induced in a magnetic field of this value have been calculated to generate electric fields of about 200 mV m^{-1} near the sino-atrial (pacemaker) node of the heart during the relative refractory period of the cardiac cycle, when cardiac excitability is relatively low.

16 NRPB concludes that acute adverse responses will not occur for exposure to static magnetic fields of less than 2 T.

17 There is insufficient evidence from animal and cellular studies to determine long-term health effects due to chronic exposure to static magnetic fields.

Occupational exposure

18 On the basis of the evidence on acute effects, and the uncertainty concerning long-term effects, NRPB considers a cautious approach to restricting exposure to static magnetic fields is merited.

19 NRPB concludes that restricting whole-body time-weighted average exposure to a magnetic flux density of 200 mT is appropriate for occupational exposure to static magnetic fields with an instantaneous ceiling of 2 T. For exposure of the limbs, a ceiling of 5 T is appropriate.

General public exposure

20 NRPB supports the cautious approach adopted by ICNIRP in setting its basic restrictions on static magnetic fields for the general public, ie a time-weighted average magnetic flux density of 40 mT for whole-body exposure.

21 NRPB considers that exposures in excess of 40 mT are appropriate for occasional access to special facilities under controlled conditions provided that the occupational exposure restrictions are not exceeded.

Recommendation

22 The ICNIRP exposure guidelines should be used for restricting occupational and general public exposure to static magnetic fields (see Appendix C).

ELECTRIC AND MAGNETIC FIELDS OF FREQUENCIES BELOW 100 kHz

23 The most plausible and coherent set of data from which guidance can be developed concerns weak electric field interactions in the CNS and certain other electrically excitable tissues. A cautious approach has been used to indicate thresholds for adverse health effects that are scientifically plausible. Data on other possible health effects examined lack plausibility, coherence and consistency. There is a need for key uncertainties in these data to be addressed through further research and scientific discussion.

24 The primary means by which the induced electric fields and currents interact with biological tissue is through voltage-gated ion channels situated in cell membranes. The effect is to alter the flux of certain ions, and the electric potential, across the cell membrane leading to subsequent biological responses. The most sensitive tissues are those comprising interacting networks of electrically excitable tissue, such as the

central, autonomic and enteric nervous systems. The heart, other muscle tissue and 'non-excitable' tissues with voltage-sensitive ion channels are expected to show a lower sensitivity.

25 Thresholds of around 100 mV m^{-1}, possibly as low as 10 mV m^{-1}, have been identified for effects in the central, autonomic and enteric nervous systems, spanning the range identified in Appendix A for most adults and for potentially susceptible individuals. However, it is recognised that there is considerable uncertainty associated with these values, which is not possible to resolve without further experimental and dosimetric investigation. It is considered appropriate to apply these threshold values over a broad frequency range (approximately 10 Hz – 1 kHz) and to a minimum of around 1000 interacting cells, which would occupy approximately 1 mm^3 in tissue of the CNS.

26 Precise comparison of basic restrictions expressed in terms of induced electric field strength with those expressed in terms of induced current density requires computational modelling employing tissue- and frequency-dependent values of electrical conductivity. In the absence of such data, simple comparisons can be made with existing guidelines assuming a fixed chosen value of electrical conductivity.

27 When a person is in an electric field, is ungrounded and comes into contact with a grounded object there is the possibility of occurrence of a spark discharge at the point of contact between the person and the object. For fields external to the body greater than about 5 kV m^{-1}, there is the likelihood of such discharges being painful. The extent to which this is a problem in practice is unclear and further investigation is merited.

28 When a person is in an electric field and comes into contact with an ungrounded object there is the possibility of occurrence of a spark discharge at the point of contact between the object and the person. For such situations, the probability and the magnitude of the effect depend on the field strength and the size of the ungrounded object.

Occupational exposure

29 NRPB concludes that a restriction of the induced electric field in the tissue of the central, autonomic and enteric nervous systems to less than 100 mV m^{-1} is adequate to protect most adult members of the population*.

30 The value of 100 mV m^{-1} was derived primarily from a consideration of weak electric field effects in the CNS and corresponds approximately to the existing ICNIRP basic restriction on current density of 10 mA m^{-2}, assuming an electrical conductivity value of CNS tissue of 0.1 S m^{-1}.

31 NRPB concludes that 10 mA m^{-2} is an appropriate basic restriction on induced current density in the CNS for occupational exposure.

General public exposure

32 In respect of general public exposure, those exposed might include people potentially susceptible to electrical stimulation, ie people with epilepsy, a family history of seizure, or using tricyclic anti-depressants, neuroleptic agents and other drugs that

* It is acknowledged that setting aside the lower range of uncertainty, based on phosphene data, facilitates international harmonisation. A cautious approach is nevertheless maintained at power frequencies and above through the application of a flat frequency response between 10 and 1000 Hz.

lower seizure threshold. It should be noted that some workers may have these conditions, and that seizure is a CNS phenomenon, not autonomic or enteric. The ad hoc expert group (Appendix A) considered that such sensitive people should be adequately protected at lower induced electric field strengths, possibly about a factor of five lower than for normal adults. In addition, the group considered that this reduction factor would be adequate to protect the developing nervous system *in utero*, and in neonates and young children. NRPB concludes that a restriction of the induced electric field in the tissue of the CNS to less than 20 mV m^{-1} is adequate to protect these members of the population.

33 The value of 20 mV m^{-1} was derived from a consideration of weak electric field effects in the CNS and corresponds approximately to the existing ICNIRP basic restriction on current density of 2 mA m^{-2}, assuming an electrical conductivity value of CNS tissue of 0.1 S m^{-1}.

34 NRPB concludes that 2 mA m^{-2} is an appropriate basic restriction on induced current density in the CNS for general public exposure.

Reference levels

35 Calculations have been carried out by NRPB, to judge the appropriateness of the reference levels for occupational and general public exposure to electric and magnetic fields of frequencies less than 100 kHz (Figures 1 and 2). These calculations indicate that the reference levels are appropriate for use at the initial stage of assessing compliance with the relevant basic restrictions on induced current density.

Recommendations

36 The ICNIRP basic restrictions on induced current density should be used for restricting occupational and general public exposure to electric and magnetic fields of frequencies less than 100 kHz.

37 The ICNIRP reference levels should be used at the initial stage of assessing compliance with basic restrictions on exposure.

38 Further investigations of compliance, that are indicated by exceeding these reference levels, should use the most up to date dosimetry data.

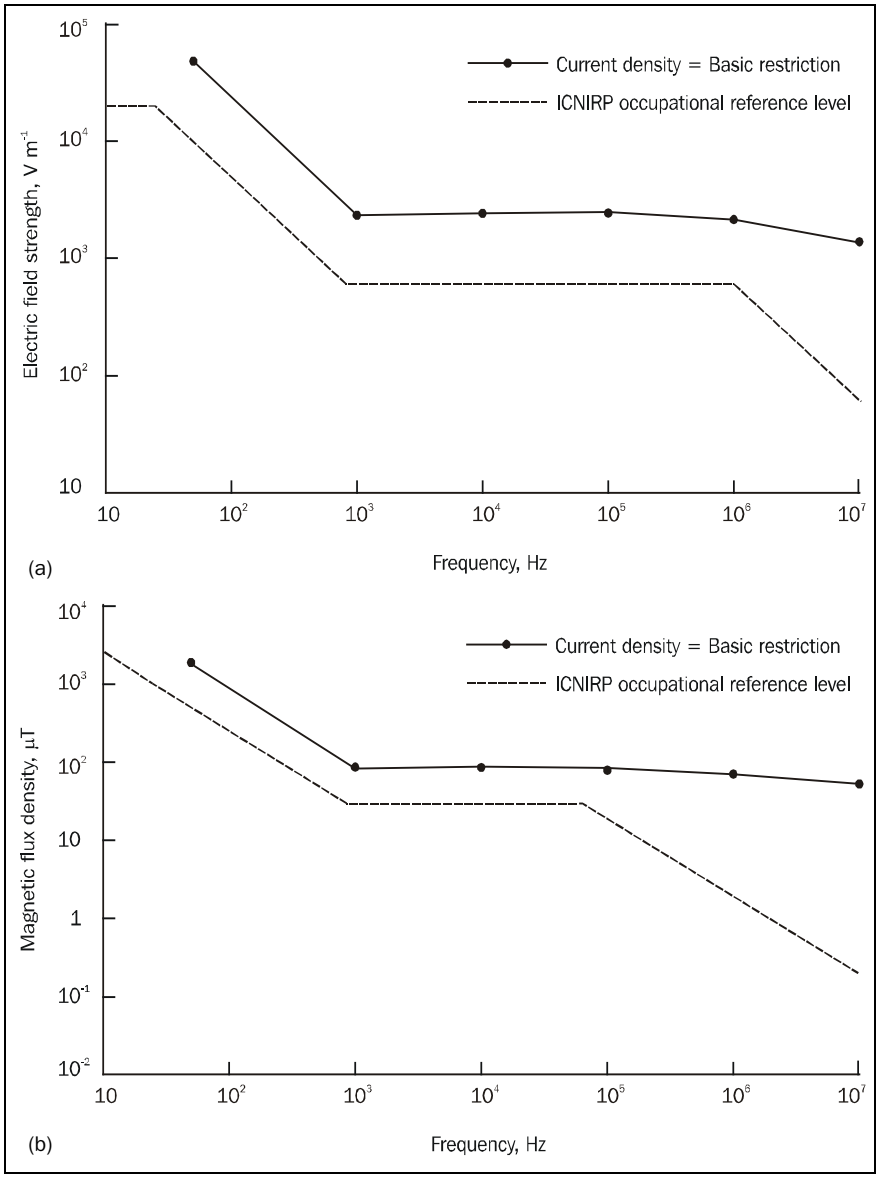
TIME-VARYING EMFS OF FREQUENCIES ABOVE 100 kHz

39 The most plausible and coherent set of data from which guidance can be developed concerns raised temperatures and the physiological stress induced by increased heat loads. A cautious approach has been used to derive thresholds for adverse health effects that are scientifically plausible. Other studies reviewed lack plausibility, coherence and consistency. There is a need for key uncertainties in these data to be addressed through further research. In particular, the distribution of increased sensitivity to the effects of heat in members of the population is not well defined at present.

40 The exposure metric for restricting exposure to fields of frequencies between 100 kHz and 10 GHz is specific energy absorption rate (SAR), unit W kg^{-1}. For frequencies between 10 and 300 GHz, because of diminishing penetration into the body, the exposure metric is incident power density, unit W m^{-2}.

FIGURE 1

(a) Comparison of the ICNIRP occupational reference level and NRPB quasistatic calculations of the electric field strength required to produce a current density equal to the ICNIRP basic restriction on induced current density with averaging over 1 cm^2 in the brain, spinal cord and retina



(b) Comparison of the ICNIRP occupational reference level and NRPB quasistatic calculations of the magnetic flux density required to produce a current density equal to the ICNIRP basic restriction on induced current density with averaging over 1 cm^2 in the brain, spinal cord and retina

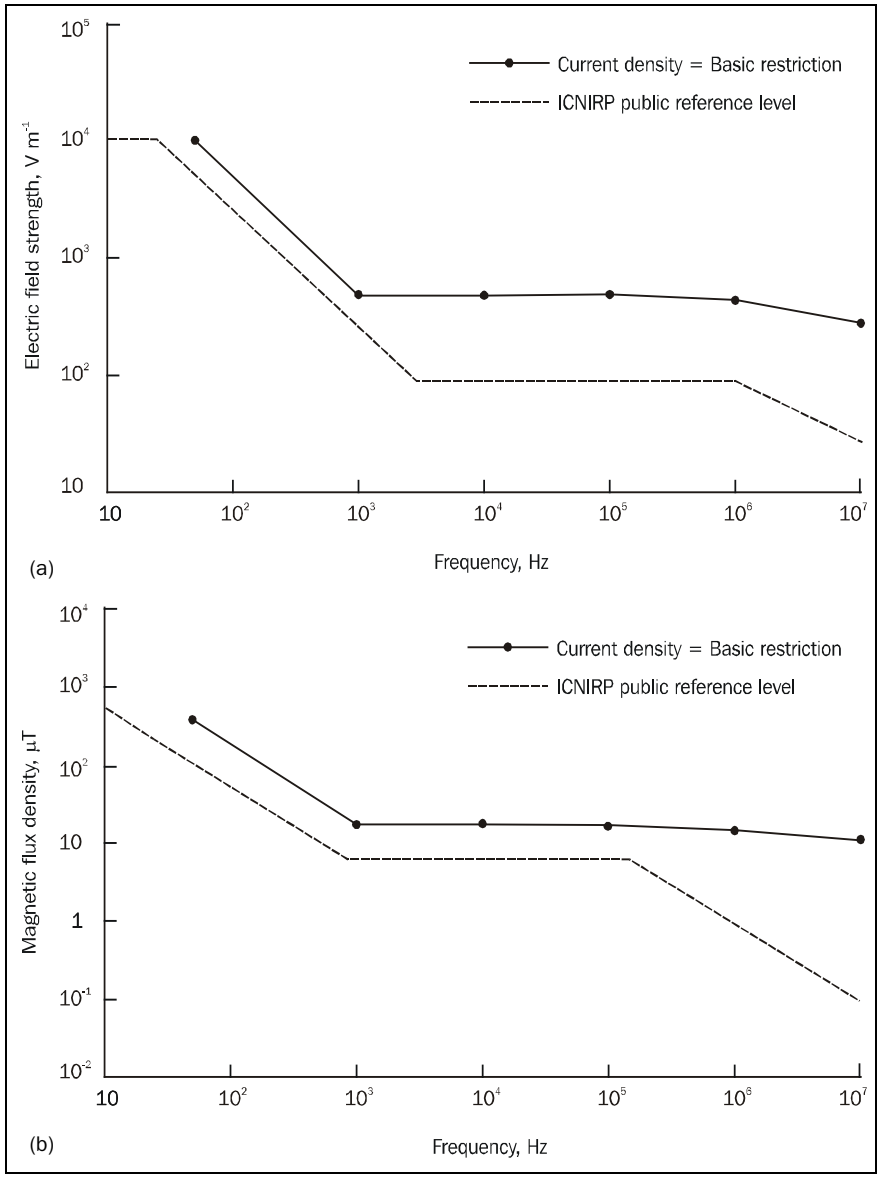


FIGURE 2

(a) *Comparison of the ICNIRP general public reference level and NRPB quasistatic calculations of the electric field strength required to produce a current density equal to the ICNIRP basic restriction on induced current density with averaging over 1 cm^2 in the brain, spinal cord and retina*

(b) *Comparison of the ICNIRP general public reference level and NRPB quasistatic calculations of the magnetic flux density required to produce a current density equal to the ICNIRP basic restriction on induced current density with averaging over 1 cm^2 in the brain, spinal cord and retina*

Occupational exposure

Whole-body

41 NRPB considers that limiting whole-body radiofrequency (RF) induced heat load to less than 0.4 W kg^{-1} will prevent heat-related disorders. For most adults it is unnecessary to additionally account for high rates of physical work and/or hot, humid environments.

Partial-body

42 With regard to partial-body (localised) heating, limiting the rise in the temperature of the head and spinal cord, to 38°C; of the other tissues of the neck and trunk (with the exception of the testes) to 39°C; and of the limbs to 40°C, should avoid any heat induced damage in the tissues of these regions of the body. For the testes, the increase in temperature should be limited to 1°C, because of their greater sensitivity to heat. NRPB concludes that occupational basic restrictions on exposure should be aimed at limiting localised temperature rises to these values.

43 There are still relatively few dosimetric studies linking localised temperature increases and SAR in most parts of the body. However, with respect to exposure of the head from the use of mobile phones, there is a growing body of computational work available. These studies provide reassurance as to the very low localised temperature increases that might arise from the use of a mobile phone and insight on the relationship between temperature rise and SAR in this case. The results indicate a range of localised temperature increases of 0.05 to 0.12°C in the brain from a localised SAR of 1 W kg^{-1}. The highest of this range of values indicates that, in order to limit the temperature in all parts of the brain to 38°C (corresponding to a temperature rise of 1°C above baseline), the SAR in the head, averaged over any 10 g cube, should not exceed about 8 W kg^{-1}.

44 Studies of heating in the eye suggest that an SAR of 1 W kg^{-1} averaged over the eye may lead to a temperature rise of up to 0.25°C in the region of the lens. Therefore, these studies indicate that in order to limit the temperature in the eye to 39°C, the SAR averaged over 10 g should be limited to about 8 W kg^{-1}.

45 Calculations on possible temperature rises in the head and eye indicate the need to restrict localised SAR to about 8 W kg^{-1} averaged over a 10 g cube. These calculations also indicate that the highest average SAR over any contiguous 10 g mass is typically at least 50% greater than this. Adequate protection is therefore afforded by restricting localised SAR in the head and trunk to 10 W kg^{-1} averaged over any contiguous 10 g mass. However, given the range of published dosimetric data relating temperature rise with localised SAR, further dosimetric studies addressing this topic should be carried out.

Reference levels

46 Calculations have been carried out by NRPB, to judge the appropriateness of the ICNIRP external power density and limb current reference levels for occupational exposure to plane wave EMFs of frequencies greater than 100 kHz (see Figure 3). These indicate that, to different degrees, the reference levels for occupational exposure are appropriate for use at the initial stage of assessing compliance with basic restrictions on SAR.

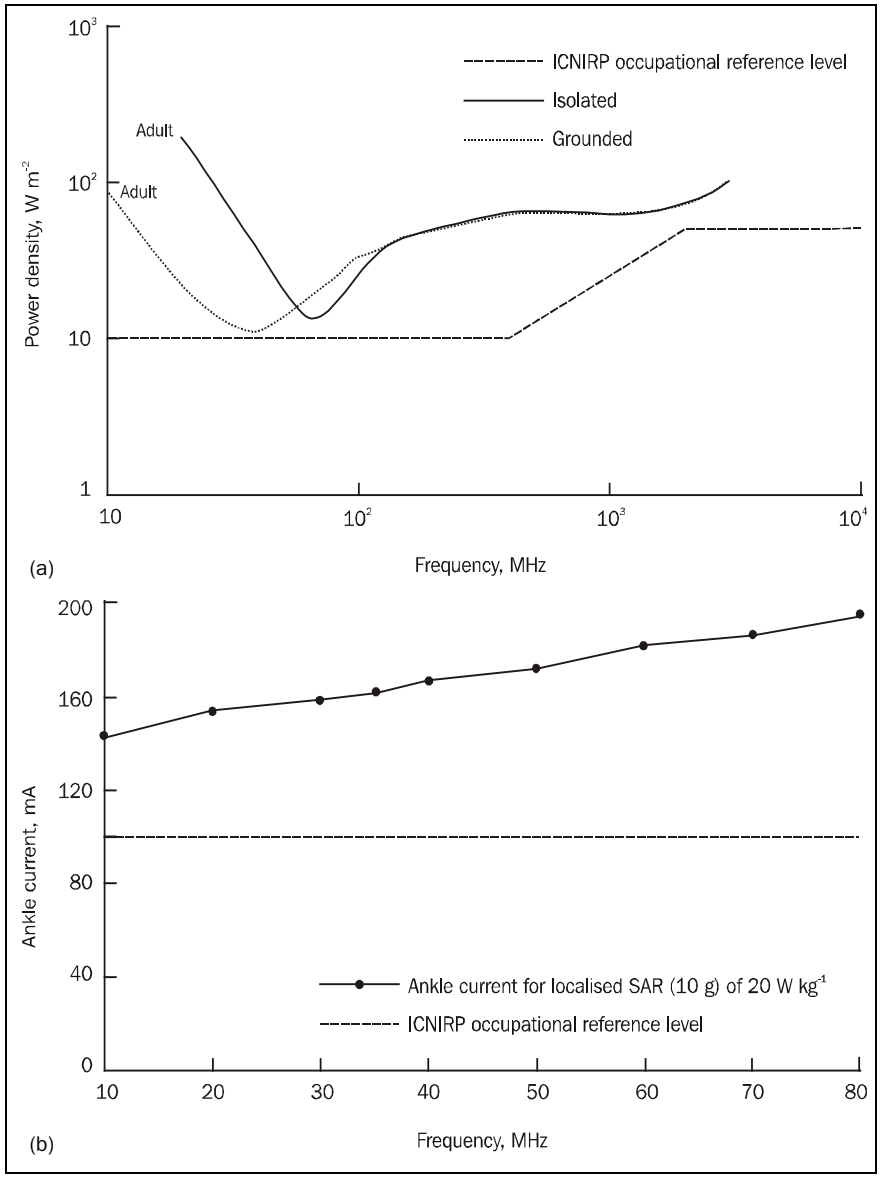


FIGURE 3

(a) *Comparison of the ICNIRP occupational reference level and NRPB plane wave calculations of the power density required to produce a whole-body SAR equal to the ICNIRP basic restriction*

(b) *Comparison of the ICNIRP occupational reference level and NRPB calculations of the induced ankle current required to produce a maximum localised SAR averaged over 10 g anywhere in the leg equal to the corresponding ICNIRP basic restriction*

General public exposure

Whole-body

47 General community protection, including for people potentially susceptible to heat related disorders, will be assured if the whole-body RF heat load is below an SAR of about 0.1 W kg^{-1}. This will provide protection to older people, infants, children, pregnant women, other adults taking certain medications and to people undertaking cognitively demanding tasks.

48 For frequencies between 100 kHz and 10 GHz this agrees reasonably well with the ICNIRP exposure guidelines basic restriction of 0.08 W kg^{-1} for the general public.

Partial-body

49 With regard to partial-body (localised) heating, limiting the rise in temperature of the head and spinal cord, and of the embryo and fetus, to 38°C; of the other tissues of the neck and trunk (with the exception of the testes) to 39°C; and of the limbs to 40°C, should avoid heat induced damage in the tissues of these regions of the body. For the testes, the increase in temperature should be limited to 1°C, because of their greater sensitivity to heat. NRPB concludes that general public basic restrictions on exposure should be aimed at limiting localised temperature rises to these values.

50 Computational studies have been published on temperature rises that might arise from exposure of the head associated with the use of mobile phones. These studies provide insight on possible temperatures that could result from a localised SAR of 2 W kg^{-1} averaged over 10 g mass of tissue. This value is one that has been adopted by ICNIRP as a basic restriction on localised SAR in the head and trunk for general public exposure and recommended by the Independent Expert Group on Mobile Phones (IEGMP), the Department of Health and the Board of NRPB as being appropriate for restricting exposure associated with mobile telephony. Computational results indicate localised temperature increases of up to around 0.2–0.25°C could result in the brain from a localised SAR of 2 W kg^{-1}. Little work has been carried out on thermal dosimetry of the fetus or with computational models incorporating reduced organ perfusion rates as might be relevant to people with cardiovascular or other diseases.

51 Taking into account uncertainties related to partial-body exposure, the above conclusions on limiting temperature increases associated with general public exposure to fields of frequencies between 100 kHz and 10 GHz agree reasonably well with the current ICNIRP basic restriction on localised SAR (2 W kg^{-1}) and with the recommendations for restricting exposure associated with mobile telephony from IEGMP and the Board of NRPB.

Reference levels

52 Calculations have been carried out by NRPB, to judge the appropriateness of the external power density and limb current reference levels for general public exposure to plane wave EMFs of frequencies greater than 100 kHz (see Figure 4). They suggest that the ICNIRP reference levels for general public exposure are generally conservative for assessing compliance with basic restrictions on SAR. However, the exception is for the exposure of small children under worst-case exposure conditions at frequencies between about 50 and 100 MHz and above about 1 GHz.

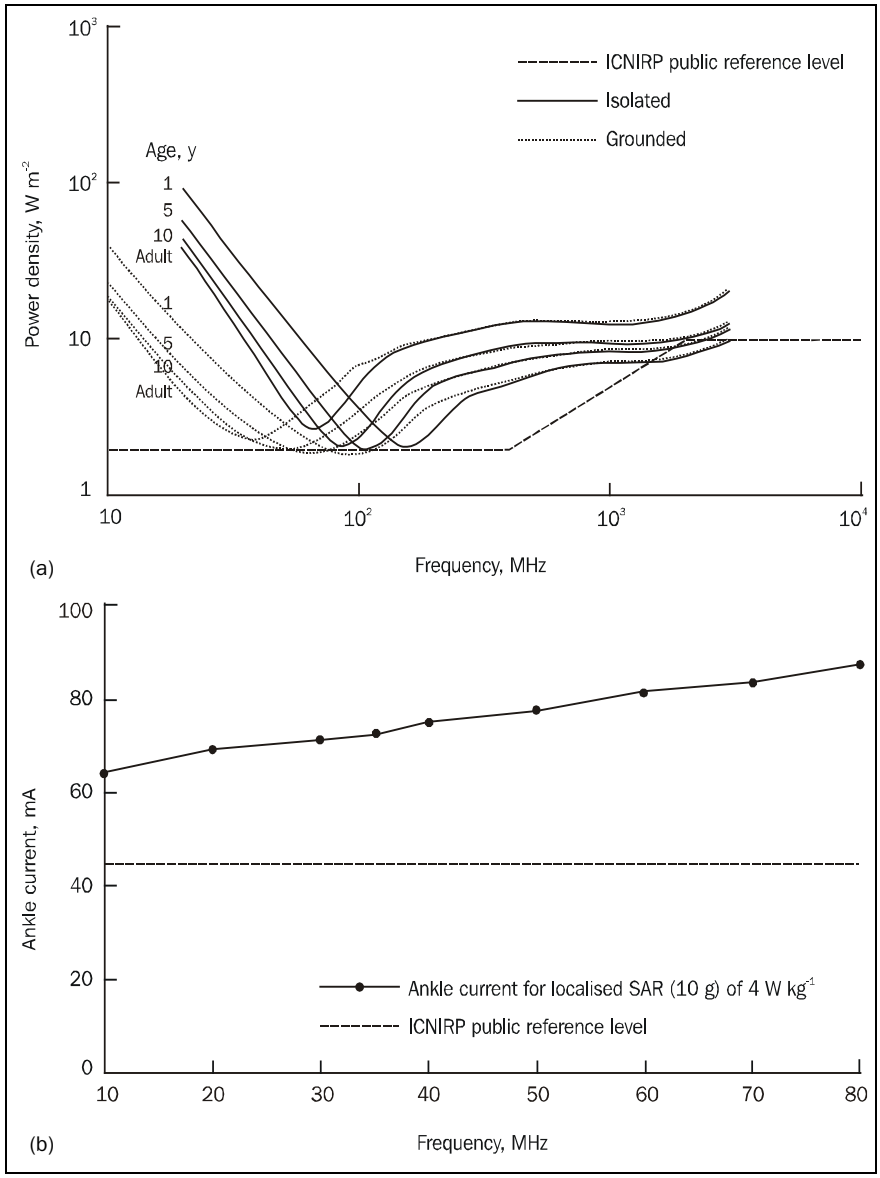


FIGURE 4

(a) *Comparison of the ICNIRP general public reference level and NRPB plane wave calculations of the power density required to produce a whole-body SAR equal to the ICNIRP basic restriction*

(b) *Comparison of the ICNIRP general public reference level and NRPB calculations of the induced ankle current required to produce a maximum localised SAR averaged over 10 g anywhere in the leg equal to the corresponding ICNIRP basic restriction*

53 NRPB considers that the appropriateness of the field reference levels for exposure of the general public needs to be reviewed for frequencies between about 50 and 100 MHz and above 1 GHz. Nevertheless, given the conservative assumptions used to derive the basic restrictions for the general public and the assumption of optimal coupling to the field in deriving the reference levels, it is considered appropriate to use the ICNIRP reference levels at present.

Recommendations

54 The ICNIRP basic restrictions on whole-body and localised SAR should be used for restricting occupational and general public exposure to EMFs of frequencies greater than 100 kHz.

55 Electrical effects on body tissues are also possible at frequencies above 100 kHz and up to about 10 MHz; hence basic restrictions to prevent these effects should apply up to 10 MHz.

56 The ICNIRP reference levels should be used at the initial stage of assessing compliance with basic restrictions on exposure.

57 Further investigations of compliance, that are indicated by exceeding these reference levels, should use the most up to date dosimetry data.

FURTHER PRECAUTIONARY MEASURES

58 The background and indicators for considering the possible need for further precautionary measures are discussed in Chapter 6.

Power frequency fields

59 There remain concerns about possible effects of exposure of children to power frequency magnetic fields. The view of NRPB is that it is important to consider the possible need for further precautionary measures in respect of exposure of children to power frequency magnetic fields.

Radiofrequency fields

60 With respect to RF exposures and health, NRPB noted the conclusions of the AGNIR report on RF fields and human health (AGNIR, 2003).

61 NRPB concludes that the scientific evidence for RF fields causing adverse health effects at levels to which the generally public are normally exposed is much weaker than that for power frequency magnetic fields. It also notes there is a great deal of ongoing scientific research on RF fields, in particular on mobile telephony, and health. There is a need to constantly monitor the results of this research and keep the guidelines under review.

Recommendation

62 The government should consider the need for further precautionary measures in respect of exposure of people to EMFs. In doing so, it should note that the overall evidence for adverse effects of EMFs on health at levels of exposure normally experienced by the general public is weak. The least weak evidence is for the exposure of children to power frequency magnetic fields and childhood leukaemia.

FUTURE DEVELOPMENT OF EXPOSURE GUIDELINES

63 Recommendations for studies of the possible effects of EMF exposure, including epidemiological studies, especially in relation to cancer, reproductive and behavioural effects, have been given in a number of recent reviews (eg AGNIR, 2001a,c, 2003; Ahlbom et al, 2001). The following recommendations are specifically aimed at developing guidance through research in key areas where continuing uncertainty limits the rigour with which appropriate restrictions on exposure can be formulated.

Static magnetic fields

64 Epidemiological studies should be carried out of the long-term risks to health of prolonged occupational exposure to static magnetic fields. Additional studies of occupational health, for example using questionnaires, to derive indices of health status should also be considered. These studies in human populations should be complemented by long-term animal studies in static fields in excess of 2 T.

65 Further study should be carried out of the potential long-term effects of static magnetic fields greater than 1 T on potentially susceptible metabolic reactions, such as those in which radical pairs are transiently generated. These should be complemented by volunteer and *in vitro* studies of magnetic field induced changes in metabolism using modern, molecular approaches such as genomics, proteomics and metabolomics.

66 The degree to which vertigo, nausea and other acute effects are a feature of occupational exposure to fields in excess of 2 T should be investigated.

Power frequency surface charge effects

67 Further exploration of the thresholds for surface electric charge effects induced by exposure to power frequency electric fields should be carried out in both occupational situations and those encountered by the general public.

Weak induced electric field effects

68 The susceptibility of the brain and other electrically excitable tissue to weak electric field interactions remains largely unexplored. Further study of the mechanism of phosphene induction and its frequency response through neurophysiological investigation of induced electric field effects on retinal neuronal circuitry, and similar studies of the threshold and frequency response of neural networks in other brain tissue, are required to clarify the degree to which phosphene data can be extrapolated to the rest of the brain.

69 These studies would be usefully supplemented by further macrodosimetric and microdosimetric investigation of the induced fields and currents in the retina in volunteer studies of phosphenes.

70 Volunteer studies are required to identify behavioural and cognitive functions affected by exposure. Animal models should be used to supplement these data.

71 The degree to which sensitivity may be increased in people with conditions such as epilepsy should be investigated through neurophysiological and behavioural investigation using *in vitro* and animal models of these conditions.

72 For time-varying fields of frequencies less than 100 kHz, there is a growing consensus that the appropriate dosimetric quantity with which to express basic restrictions on EMF exposure should be induced electric field strength. Such recommendations were made at an EMF Exposure Guidelines Science Workshop held in Brussels (Sheppard et al, 2000) and have been incorporated into the IEEE standard on limiting human exposure

to EMFs up to 3 kHz (IEEE, 2002). Similar recommendations were made to NRPB by an ad hoc expert group (Appendix A) and at a recent ICNIRP/WHO workshop (Appendix B; Blakemore et al, 2003). This represents a change from the practice used by many bodies concerned with the development of EMF exposure guidelines (eg ICNIRP, 1998; NRPB, 1999) where, for this frequency range, basic restrictions are expressed in terms of induced current density.

73 In the further development of EMF exposure guidelines, consideration should be given to the basic restrictions for time-varying electric and magnetic fields of frequencies up to 100 kHz being based on limiting electric field strength internal to the body.

Whole-body SAR

74 The distribution of heat sensitivity in the general population is not well understood; in particular, there is some uncertainty regarding the heat loads that people with varying susceptibilities to heat can tolerate. Raised maternal body temperature can adversely affect prenatal and possibly early postnatal development, particularly that of the CNS, but thresholds have not been rigorously identified. More quantitative studies should be carried out, especially on development of the cerebral cortex, during prenatal and postnatal exposure using both morphological and functional endpoints.

Localised SAR

75 With regard to localised heating, acute animal studies have shown that tissue necrosis can be induced when local temperatures exceed 41°C for an hour or more. Further studies should be carried out of the effects of prolonged and/or chronic exposure at lower temperatures, especially those that might result from functional changes induced, for example, by heating of the brain or endocrine glands.

76 For exposure to mobile phones, there are conflicting reports as to whether there is a significant increase in the SAR absorbed in the head, and particularly in the brain, for children compared to adults. This is an area where clarification is needed.

77 Further work should be carried out to provide more knowledge of the quantitative relationship between localised temperature increases and SAR in the head and eye, trunk, embryo and fetus including using models incorporating reduced organ blood perfusion rate. Particular attention should be given to the acquisition of reliable measurements of the thermal parameters of human tissues, including perfusion rates.

78 The metric used in the ICNIRP guidelines – the SAR average over any 10 g of contiguous tissue – does not distinguish between compact and diffuse patterns of heating which are likely to have different thermal effects. The consequences of a cubic averaging region for exposure guidelines should be investigated.

Dosimetry and reference levels

79 An important requirement in future dosimetry is the development of an adult female voxel model and also child models which are not simply scaled adults, along with the appropriate age-dependent tissue dielectric parameters.

80 The appropriateness of the field reference levels for exposure of the general public needs to be reviewed for frequencies between about 50 and 100 MHz and above 1 GHz (see paragraphs 52 and 53).

81 Induced electric fields need to be calculated averaged over a 1 mm cube in the brain, spinal cord and retina for low frequency electric and magnetic field exposures.

8 References

Adair R K (1999). Effects of very weak magnetic fields on radical pair reformation. *Bioelectromagnetics,* **20**(4), 255–63.

Adair R K (2001). Simple neural networks for the amplification and utilisation of small changes in neuron firing rates. *Proc Natl Acad Sci (USA),* **98**(13), 7253–8.

Adair E R and Berglund L G (1986). On the thermoregulatory consequences of NMR imaging. *Magn Reson Imaging,* **4**, 321–33.

Adair E R and Black D R (2003). Thermoregulatory responses to RF energy absorption. *Bioelectromagnetics,* **Suppl 6**, S17–38.

Adair R K, Astumian R D and Weaver J C (1998a). Detection of weak electric fields by sharks, rays and skates. *Chaos,* **8**(3), 576–87.

Adair E R, Cobb B L, Mylacraine K S and Kelleher S A (1999). Human exposure at two radio frequencies (450 and 2450 MHz): similarities and differences in physiological response. *Bioelectromagnetics,* **20**, 12–20.

Adair E R, Kelleher S A, Mack G W and Morocco T S (1998b). Thermophysiological responses of human volunteers during controlled whole-body radiofrequency exposure at 450 MHz. *Bioelectromagnetics,* **19**, 232–45.

Adair E R, Mylacraine K S and Cobb B L (2001a). Partial-body exposure of human volunteers to 2450 MHz pulsed or CW fields provokes similar thermoregulatory responses. *Bioelectromagnetics,* **22**, 246–59.

Adair E R, Mylacraine K S and Cobb B L (2001b). Human exposure to 2450 MHz CW energy at levels outside the IEEE C95.1 standard does not increase core temperature. *Bioelectromagnetics,* **22**, 429–39.

Adey W R, Byus C V, Cain C D, Higgins R J, Jones R A, Kean C J, Kuster N, MacMurray A, Stagg R B, Zimmerman G, Phillips J L and Haggren W (1999). Spontaneous and nitrosurea-induced primary tumors of the central nervous system in Fischer 344 chronically exposed to 836 MHz modulated microwaves. *Radiat Res,* **152**, 293–302.

Adey W R, Byus C V, Cain C D, Higgins R J, Jones R A, Kean C J , Kuster N, MacMurray A, Stagg R B and Zimmerman G (2000). Spontaneous and nitrosourea-induced primary tumors of the central nervous system in Fischer 344 rats exposed to frequency-modulated microwave fields. *Cancer Res,* **60**, 1857–63.

Adrian D J (1977). Auditory and visual sensations induced by low-frequency electric currents. *Radio Sci,* **12**, 243–50.

Afzal S M J and Liburdy R P (1998). Magnetic fields reduce the growth inhibitory effects of tamoxifen in a human brain tumor cell line. IN *Electricity and Magnetism in Biology and Medicine* (F Bersani, ed). Bologna, Plenum Press.

AGNIR (1992). Electromagnetic fields and the risk of cancer. Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* **3**(1), 1–138.

AGNIR (1994). Health effects related to the use of visual display units. Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* **5**(2), 1–75.

AGNIR (2001a). ELF electromagnetic fields and the risk of cancer. Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* **12**(1), 1–179.

AGNIR (2001b). ELF electromagnetic fields and neurodegenerative disease. Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* **12**(4), 1–24.

AGNIR. (2001c) Possible health effects from terrestrial trunked radio (TETRA). Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* (**12**)2, 1–86.

AGNIR (2002). Magnetic fields and miscarriage. Statement by the Advisory Group on Non-ionising Radiation. http://www.nrpb.org/publications/bulletin/no1/article1.htm.

AGNIR (2003). Health effects from radiofrequency electromagnetic fields. Report of an Advisory Group on Non-ionising Radiation. *Doc NRPB,* **14**(2), 1–177.

AGNIR (2004). Particle deposition in the vicinity of power lines and possible effects on health. Report of an independent Advisory Group on Non-ionising Radiation and its Ad Hoc Group on Corona Ions. *Doc NRPB,* **15**(1), 1–55.

Ahlbom, A (2001). Neurodegenerative diseases, suicide and depressive symptoms in relation to EMF. *Bioelectromagnetics,* **Suppl 5**, S132–43.

Ahlbom A, Day N, Feychting M, Roman E, Skinner J, Dockerty J, Linet M, McBride M, Michaelis J, Olsen J H, Tynes T and Verkasalo P K (2000). A pooled analysis of magnetic fields and childhood leukaemia. *Br J Cancer,* **83**, 692–8.

Ahlbom A, Cardis E, Green A, Linet M, Savitz D and Swerdlow A (2001). Review of the epidemiologic literature on EMF and health. *Environ Health Perspect,* **109**(Suppl 6), 911–33.

Akerstedt T, Arnetz B, Ficca G, Paulsson L E and Kallner A (1999). A 50 Hz electromagnetic field impairs sleep. *J Sleep Res,* **8**(1), 77–81.

Al-Akhras M A, Elbetieha A, Hasan M K, Al-Omari I, Darmani H and Albiss B (2001). Effects of extremely low frequency magnetic field on fertility of adult male and female rats. *Bioelectromagnetics,* **22**(5), 340–44.

Anane R, Dulou P E, Taxile M, Geffard M, Crespeau F L and Veyret B (2003). Effects of GSM-900 microwaves on DMBA-induced mammary gland tumors in female Sprague-Dawley rats. *Radiat Res,* **160**, 492–7.

Anderson G S, Meneilly G S and Mekjavic I B (1996). Passive temperature lability in the elderly. *Eur J Appl Physiol,* **73**, 278–86.

Anderson L E, Boorman G A, Morris J E, Sasser L B, Mann P C, Grumbein S L, Hailey J R, McNally A, Sills R C and Haseman J K (1999). Effect of 13 week magnetic field exposures on DMBA-initiated mammary gland carcinomas in female Sprague-Dawley rats. *Carcinogenesis,* **20**(8), 1615–20.

Anderson L E, Morris J E, Sasser L B and Löscher W (2000). Effects of 50 or 60 hertz, 100 μT magnetic field exposure in the DMBA mammary cancer model in Sprague-Dawley rats: possible explanations for different results from two laboratories. *Environ Health Perspect,* **108**(9), 797–802.

Andersson B, Berg M, Arnetz B B, Melin, Langlet I and Liden S (1996). A cognitive-behavioral treatment of patients suffering from 'electric hypersensitivity'. Subjective effects and reactions in a double-blind provocation study. *J Occup Environ Med,* **38**(8), 752–8.

Ansari R M and Hei T K (2000). Effects of 60 Hz extremely low frequency magnetic fields (EMF) on radiation- and chemical-induced mutagenesis in mammalian cells. *Carcinogenesis,* **21**(6), 1221–6.

Antoni H (1998). Electrical properties of the heart. IN *Applied Bioelectricity: From Electrical Stimulation to Electropathology* (J P Reilly, ed). New York, Springer, Chapter 5, pp 148–93.

Antonopoulos A, Yang B, Stamm A, Heller W D and Obe G (1995). Cytological effects of 50 Hz electromagnetic fields on human lymphocytes *in vitro. Mutat Res,* **346**(3), 151–7.

Aran J-M, Bolomey J-C, Buser P, de Seze R, Hours M, Lagroye I and Veyret B (2003). Téléphonie mobile et santé. Rapport à l'Agence Française de Sécurité Sanitaire Environnementale. http://www.afsse.fr/documents/AFSSE_TM_experts.pdf.

Armstrong B (1998). Effect of measurement error on epidemiological studies of environmental and occupational exposures. *Occup Environ Med,* **55**, 651–6.

Arnetz B B (1997). Technological stress: psychophysiological aspects of working with modern information technology. *Scand J Work Environ Health,* **23**(Suppl 3), 97–103.

Arnetz B B, Berg M and Arnetz J (1997). Mental strain and physical symptoms among employees in modern offices. *Arch Environ Health,* **52**(1), 63–7.

Attwell D (2003). Interaction of low frequency electric fields with the nervous system: the retina as a model system. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 341–8.

Auvinen, A, Hietanen, M, Luukkonen, R and Koskela, R S (2002). Brain tumors and salivary gland cancers among cellular telephone users. *Epidemiology,* **13**, 356–9.

Azadniv M, Klinge C M, Gelein R, Carstensen E L, Cox C,Brayman A A and Miller M W (1995). A test of the hypothesis that a 60 Hz magnetic field affects ornithine decarboxylase activity in mouse L929 cells *in vitro. Biochem Biophys Res Commun,* **214**(2), 627–31.

Babbitt J T, Kharazi A I, Taylor J M, Bonds C B, Mirell S G, Frumkin E, Zhuang D and Hahn T J (2000). Hematopoietic neoplasia in C57BL/6 mice exposed to split-dose ionizing radiation and circularly polarized 60 Hz magnetic fields. *Carcinogenesis,* **21**(7), 1379–89.

Bailey W H and Charry J M (1986). Behavioral monitoring of rats during exposure to air ions and DC electric fields. *Bioelectromagnetics,* **7**, 329.

Bakos J, Nagy N, Thuroczy G and Szabo L D (1995). Sinusoidal 50 Hz, 500 μT magnetic field has no acute effect on urinary 6-sulphatoxymelatonin in Wistar rats. *Bioelectromagnetics,* **16**(6), 377–80.

Bakos J, Nagy N, Thuroczy G and Szabo L D (1997). Urinary 6-sulphatoxymelatonin excretion is increased in rats after 24 hours of exposure to vertical 50 Hz, 100 μT magnetic field. *Bioelectromagnetics,* **18**(2), 190–92.

Bakos J, Nagy N, Thuroczy G and Szabo L D (1999). Urinary 6-sulphatoxymelatonin excretion of rats is not changed by 24 hours of exposure to a horizontal 50 Hz, 100 μT magnetic field. *Electro-Magnetobiol,* **18**(1), 23–31.

Balcer-Kubiczek E K and Harrison G H (1985). Evidence for microwave carcinogenesis *in vitro*. *Carcinogenesis,* **6**, 859–64.

Balcer-Kubiczek E K and Harrison G H (1991). Neoplastic transformation of C3H/10T1/2 cells following exposure to 120 Hz modulated 2.45 GHz microwaves and phorbol ester tumor promoter. *Radiat Res,* **126**, 65–72.

Balcer-Kubiczek E K, Zhang X F, Harrison G H, McCready W A, Shi Z M, Han L H, Abraham J M, Ampey L L 3rd, Meltzer S J, Jacobs M C and Davis C C (1996). Rodent cell transformation and immediate early gene expression following 60 Hz magnetic field exposure. *Environ Health Perspect,* **104**(11), 1188–98.

Balcer-Kubiczek E K, Zhang X F, Han L H, Harrison G H, Davis C C, Zhou X J, Loffe V, McCready W A, Abraham J M and Meltzer S J (1998). BIGEL analysis of gene expression in HL60 cells exposed to X rays or 60 Hz magnetic fields. *Radiat Res,* **150**(6), 663–72.

Balmain A and Harris C C (2000). Carcinogenesis in mouse and human cells: parallels and paradoxes. *Carcinogenesis,* **21**(3), 371–7.

Balode Z (1996). Assessment of radio-frequency electromagnetic radiation by the micronucleus test in Bovine peripheral erythrocytes. *Sci Total Environ,* **180**, 81–5.

Baris D, Armstrong B G, Deadman J and Thériault G (1996). A case cohort study of suicide in relation to exposure to electric and magnetic fields among electrical utility workers. *Occup Environ Med,* **53**, 17–24.

Barnett S B, Ter Haar G R, Ziskin M C, Rott H-D, Duck F A and Maeda K (2000). International recommendations and guidelines for the safe use of diagnostic ultrasound in medicine. *Ultrasound Med Biol,* **26**(3), 355–66.

Barregard L, Jarvholm B and Ungethum E (1985). Cancer among workers exposed to strong static magnetic fields. *Lancet,* **2**(8460), 892.

Bartsch H, Bartsch C, Seebald E, Deerberg F, Dietz K, Vollrath L and Mecke D (2002). Chronic exposure to a GSM-like signal (mobile phone) does not stimulate the development of DMBA-induced mammary tumors in rats: results of three consecutive studies. *Radiat Res,* **157**, 183–90.

Battocletti J H, Salles-Cunha S, Halbach R E, Nelson J, Sances A Jr and Antonich F J (1981). Exposure of rhesus monkeys to 20 000 G steady magnetic field: effect on blood parameters. *Med Phys,* **8**, 115.

Baumgardt-Elms C, Ahrens W, Bromen K, Boikat U, Stang A, Jahn I, Stegmaier C and Jockel K H (2002). Testicular cancer and electromagnetic fields (EMF) in the workplace: results of a population-based case–control study in Germany. *Cancer Causes Control,* **13**, 895–902.

Begenisich T and Melvin J E (1998). Regulation of chloride channels in secretory epithelia. *J Membrane Biol,* **163**, 77–85.

Beischer D E and Knepton J C Jr (1964). Influence of strong magnetic fields on the electrocardiogram of squirrel monkeys (*Samiri sciureus*). *Aerosp Med,* **35**, 939.

Beischer D E and Knepton J C Jr (1966). The electroencephalogrm of the squirrel monkey *(Samiri sciurens)* in a very high magnetic field. Pensacola FL, Naval Aerospace Medical Reseach Laboratory.

Belanger K, Leaderer B, Hellenbrand K, Holford T R, McSharry J, Power M E and Bracken M B (1998). Spontaneous abortion and exposure to electric blankets and heated water beds. *Epidemiology,* **9**, 36–42.

Bell G B, Marino A A and Chesson A L (1992). Alterations in brain electrical activity caused by magnetic fields: detecting the detection process. *Electroencephalogr Clin Neurophysiol,* **83**(6), 389–97.

Bell G B, Marino A A and Chesson A L (1994a). Frequency-specific responses in the human brain caused by electromagnetic fields. *J Neurol Sci,* **123**(1–2), 26–32.

Bell G B, Marino A A and Chesson A L (1994b). Frequency-specific blocking in the human brain caused by electromagnetic fields. *Neuroreport,* **5**(4), 510–12.

Bell G B, Marino A A, Chesson A L and Struve F A (1991). Human sensitivity to weak magnetic fields. *Lancet,* **338**(8781), 1521–2.

Bellossi A (1983). No-effect of a static uniform magnetic field on mouse trypanosomiasis. *Radiat Environ Biophys,* **22**, 311.

Bellossi A (1984). The effect of a static uniform magnetic field on mice a study of methylcholanthren carcinogenesis. *Radiat Environ Biophys,* **23**, 107.

Bellossi A (1986). The effect of a static non-uniform magnetic field on mice a study of Lewis tumour graft. *Radiat Environ Biophys,* **25**, 231.

Bellossi A and Toujas L (1982). The effect of a static uniform magnetic field on mice. A study of a Lewis tumour graft. *Radiat Environ Biophys,* **20**, 153.

Beniashvili D S, Bilanishvili V G and Menabde M Z (1991). Low-frequency electromagnetic radiation enhances the induction of rat mammary tumors by nitrosomethyl urea. *Cancer Lett,* **61**(1), 75–9.

Berenger J (1994). A perfectly matcher layer for the absorption of electromagnetic waves. *J Comp Phys,* **114**, 185–200.

Bergqvist U and Vogel E (1997). Possible health implications of subjective symptoms and electromagnetic fields. A report for the European Commission, DG V, Arbete och Halsa.

Berk S G, Srikanth S, Mahajan S M and Ventrice C A (1997). Static uniform magnetic fields and amoebae. *Bioelectromagnetics,* **18**(1), 81–4.

Bernardi P, Cavagnaro M and Pisa S (1996). Evaluation of the SAR distribution in the human head for cellular phones used in a partially closed environment. *IEEE Trans Electromagn Compat,* **38**, 357–66.

Bernardi P, Cavagnaro M, Pisa S and Piuzzi E (1998). SAR distribution and temperature increase in an anatomical model of the human eye exposed to the field radiated by the user antenna in a wireless LAN. *IEEE Trans Microwave Theory Techniq,* **46**, 2074–81.

Bernardi P, Cavagnaro M, Pisa S and Piuzzi E (2000). Specific absorption rate and temperature increases in the head of a cellular-phone user. *IEEE Trans Microwave Theory Techniq,* **48**, 1118–25.

Bernhardt J H (1988). The establishment of frequency dependent limits for electric and magnetic fields and evaluation of indirect effects. *Radiat Environ Biophys,* **27**, 1–27.

Bisht K S, Moros E G, Straube W L, Baty J D and Roti Roti J L (2002). The effect of 835.62 MHz FDMA or 847.74 MHz CDMA modulated radiofrequency radiation on the induction of micronuclei in C3H 10T(1/2) cells. *Radiat Res,* **157**, 506–15.

Blaasaas K G, Tynes T, Irgens A and Lie R T (2002). Risk of birth defects by parental occupational exposure to 50 Hz electromagnetic fields: a population based study. *Occup Environ Med,* **59**, 92–7.

Blaasaas K G, Tynes T and Lie R T (2003). Residence near power lines and the risk of birth defects. *Epidemiology,* **14**, 95–8.

Black D R and Heynick L N (2003). Radiofrequency (RF) effects on blood cells, cardiac, endocrine, and immunological functions. *Bioelectromagnetics,* **Suppl 6**, S187–95.

Blackman C F, Benane S G and House D E (2001). The influence of 1.2 μT, 60 Hz magnetic fields on melatonin- and tamoxifen-induced inhibition of MCF-7 cell growth. *Bioelectromagnetics,* **22**(2), 122–8.

Blackwell R P and Saunders R D (1986). The effects of low-level radiofrequency and microwave radiation on brain tissue and animal behaviour. *Int J Radiat Biol,* **50**, 761–87.

Blakemore C, Noble D, Saunders R D, and Sienkiewicz Z J (2003). Workshop summary and concluding remarks. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 397–8.

Blank M and Soo L (1992). Threshold for inhibition of Na, K-ATPase by ELF alternating currents. *Bioelectromagnetics,* **13**(4), 329–33.

Blettner M, Sauerbrei W, Schlehofer B, Scheuchenpflug T and Friedenreich C (1999). Traditional reviews, meta-analyses and pooled analyses in epidemiology. *Int J Epidemiol,* **28**, 1–9.

Blick D W, Adair E R, Hurt W D, Sherry C J, Walters T J and Merritt J H (1997). Thresholds of microwave-evoked warmth sensations in human skin. *Bioelectromagnetics,* **18**, 403–9.

Blumenthal N C, Ricci J, Berger L, Zychlinsky A, Soloman H, Chen G G, Kuznetsov D and Dorfman R (1997). Effects of low-intensity AC and/or DC electromagnetic fields on cell attachment and induction of apoptosis. *Bioelectromagnetics,* **18**(3), 264–72.

BMA (2001). Mobile phones and health: an interim report (D Morgan, ed). A publication from the BMA science department and the board of science and education. London, British Medical Association, available at http://www.bma.org.uk.

BOHS (1990). *The Thermal Environment.* British Occupational Hygiene Society, Technical Guide No 8 (D Hughes, ed). Leeds, Science Reviews Ltd.

Boice J D and McLaughlin J K (2002). Epidemiologic studies of cellular telephones and cancer risk – a review. SSI Report 2002: 16. Stockholm, Swedish Radiation Protection Authority, available at http://www.ssi.se/english/Press_release_rapp2001_16.html.

Boorman G A, Anderson L E, Morris J E, Sasser L B, Mann P C, Grumbein S L, Hailey J R, MaNally A, Sills R C and Haseman J K (1999). Effect of 26 week magnetic field exposures in a DMBA initiation–promotion mammary gland model in Sprague-Dawley rats. *Carcinogenesis,* **20**(5), 899–904.

Boorman G A, Owen R D, Lotz W G and Galvin M J Jr (2000a). Evaluation of *in vitro* effects of 50 and 60 Hz magnetic fields in regional EMF exposure facilities. *Radiat Res,* **153**(5 Part 2), 648–57.

Boorman G A, Rafferty C N, Ward J M and Sills R C (2000b). Leukemia and lymphoma incidence in rodents exposed to low-frequency magnetic fields. *Radiat Res,* **153**(5 Part 2), 627–36.

Borbely A A, Huber R, Graf T, Fuchs B, Gallmann E and Achermann P (1999). Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram. *Neurosci Lett,* **275**(3), 207–10.

Borgens R B (1999). Electrically mediated regeneration and guidance of adult mammalian spinal axons into polymeric channels. *Neuroscience,* **91**(1), 251–64.

Bornhausen M and Scheingraber H (2000). Prenatal exposure to 900 MHz, cell-phone electromagnetic fields had no effect on operant-behavior performances of adult rats. *Bioelectromagnetics,* **21**, 566–74.

Bortkiewicz A, Pilacik B, Gadzicka E, and Szymczak W (2002). The excretion of 6-hydroxymelatonin sulfate in healthy young men exposed to electromagnetic fields emitted by cellular phone – an experimental study. *Neuroendocrinol Lett,* **23 Suppl 1**, 88–91.

Bourland J B, Nyenhuis J A and Schaefer D J (1999). Physiologic effects of intense MR imaging gradient fields. *Neuroimaging Clinics of North America,* **9**(2), 363–77.

Bracken M B, Belanger K, Hellenbrand K, Dlugosz L, Holford T R, McSharry J E, Addesso K and Leaderer B (1995). Exposure to electromagnetic fields during pregnancy with emphasis on electrically heated beds: association with birthweight and intrauterine growth retardation. *Epidemiology,* **6**, 263–70.

Bradford Hill A (1965). The environment and disease: association or causation? *Proc Roy Soc Med,* **58**, 295–300.

Brady J V and Reiter R J (1992). Neurobehavioral effects. IN Health effects of low-frequency electric and magnetic fields. Oak Ridge Associated Universities, ppVII-1–40.

Braune S, Wrocklage C, Raczek J, Gailus T and Lucking C H (1998). Resting blood pressure increase during exposure to a radio-frequency electromagnetic field. *Lancet,* **351**(9119), 1857–8.

Braune S, Riedel A, Schulte-Monting J and Raczek J (2002). Influence of a radiofrequency electromagnetic field on cardiovascular and hormonal parameters of the autonomic nervous system in healthy individuals. *Radiat Res,* **158**(3), 352–6.

Brendel H, Niehaus M and Lerchl A (2000). Direct suppressive effects of weak magnetic fields (50 Hz and $16^2/_3$ Hz) on melatonin synthesis in the pineal gland of Djungarian hamsters (*Phodopus sungorus*). *J Pineal Res,* **29**, 228–33.

Brent R L (1999). Reproductive and teratologic effects of low-frequency electromagnetic fields: a review of *in vivo* and *in vitro* studies using animal models. *Teratology,* **59**(4), 261–86.

Brent R L, Gordon W E, Bennett W R and Beckman D A (1993). Reproductive and teratologic effects of electromagnetic fields. *Reprod Toxicol,* **7**(6), 535–80.

Brinck H and Werner J (1994). Efficiency function: improvement of classical bioheat approach. *J Appl Physiol,* **77,** 1617–22.

Brocklehurst B (1997). Magnetic isotope effects in biology: a marker for radical pair reactions and electromagnetic field effects? *Int J Radiat Biol,* **72**(5), 587–96.

Brocklehurst B and McLauchlan K A (1996). Free radical mechanism for the effects of environmental electromagnetic fields on biological systems. *Int J Radiat Biol,* **69**(1), 3–24.

Brusick D, Albertini R, McRee D, Peterson D, Williams G, Hanawalt P and Preston J (1998). Genotoxicity of radiofrequency radiation. *DNA/Genetox Expert Panel Environ Mol Mutagen,* **32**, 1–16.

Buemi M, Marino D, Di Pasquale G, Floccari F, Senatore M, Aloisi C, Grasso F, Mondio G, Perillo P, Frisina N and Corica F (2001). Cell proliferation/cell death balance in renal cell cultures after exposure to a static magnetic field. *Nephron,* **87**(3), 269–73.

Burch J B, Reif J S, Yost M G, Keefe T J and Pitrat C A (1998). Nocturnal excretion of a urinary melatonin metabolite among electric utility workers. *Scand J Work Environ Health,* **24**, 183–9.

Burch J B, Reif J S, Yost M G, Keefe T J and Pitrat C A (1999). Reduced excretion of a melatonin metabolite in workers exposed to 60 Hz magnetic fields. *Am J Epidemiol,* **150**, 27–36.

Burch J B, Reif J S, Noonan C W and Yost M G (2000). Melatonin metabolite levels in workers exposed to 60 Hz magnetic fields: work in substations and with 3-phase conductors. *J Occup Environ Med,* **42**, 136–42.

Byus C V and Hawel L (1997). Additional considerations about bioeffects. IN *Mobile Communications Safety* (Q Balzano and J C Lin, eds). London, Chapman and Hall, pp 133–44.

Byus C V, Kartun K, Pieper S and Adey W R (1988). Increased ornithine decarboxylase activity in cultured cells exposed to low energy modulated microwave fields and phorbol ester tumor promoters. *Cancer Res,* **48**, 4222–6.

Cahalan M D, Wulff H and Chandy K G (2001). Molecular properties and physiological roles of ion channels in the immune system. *J Clin Immunol,* **21**(4), 235–52.

Cain C D, Thomas D L and Adey W R (1997). Focus formation of C3H/10T1/2 cells and exposure to a 836.55 MHz modulated radiofrequency field. *Bioelectromagnetics,* **18**, 237–43.

Cantoni O, Sestili P Fiorani M and Dacha M (1996). Effect of 50 Hz sinusoidal electric and/or magnetic fields on the rate of repair of DNA single strand breaks in cultured mammalian cells exposed to three different carcinogens: methylmethane sulphonate, chromate and 254 nm UV radiation. *Biochem Mol Biol Int,* **38**(3), 527–33.

Cantoni O, Sestili P, Fiorani M and Dacha M (1995). The effect of 50 Hz sinusoidal electric and/or magnetic fields on the rate of repair of DNA single/double strand breaks in oxidatively injured cells. *Biochem Mol Biol Int,* **37**(4), 681–9.

Caputa K, Dimbylow P J, Dawson T W and Stuchly M A (2002). Modeling fields induced in humans by 50/60 Hz magnetic fields: reliability of the results and effects of model variations. *Phys Med Biol,* **47**(8), 1391–8.

Carnes K I and Magin R L (1996). Effects of *in utero* exposure to 4.7 T MR imaging conditions on fetal growth and testicular development in the mouse. *Magn Reson Imaging,* **14**(3),263–74.

Carpenter R H S (1972). Electrical stimulation of the eye in different adaptational states. *J Physiol,* **221**, 137–48.

Carstensen E L, Buettner A, Genberg V L and Miller M W (1985). Sensitivity of the human eye to power frequency electric fields. *IEEE Trans Biomed Eng,* **32**, 561–5.

Catterall W A (1995). Structure and function of voltage-gated ion channels. *Ann Rev Biochem,* **64**, 493–531.

Catterall W A (2000). Structure and regulation of voltage-gated Ca^{2+} channels. *Ann Rev Cell Devel Biol,* **16**, 521–55.

CEU (1999). Council Recommendation of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0 Hz to 300 GHz). *Off J Eur Commun,* **L199**, 59 (1999/519/EC). http://europa.eu.int/comm/health/ph/programmes/pollution/ph_fields_cr_en.pdf.

Chagnaud J-L, Moreau J-M and Veyret B (1999). No effect of short-term exposure to GSM-modulated low-power microwaves on benzo(a)pyrene-induced tumours in rat. *Int J Radiat Biol,* **75**, 1251–6.

Chakeres D W, Bornstein R and Kangarlu A (2003a). Randomised comparison of cognitive function in humans at 0 and 8 T. *J Magn Reson Imaging,* **18**, 342–5.

Chakeres D W, Kangarlu A, Boudoulas H, and Young D C (2003b). Effect of static magnetic field exposure of up to 8 T on sequential human vital sign measurements. *J Magn Reson Imaging,* **18**, 346–52.

Charles L E, Loomis D, Shy C M, Newman B, Millikan R, Nylander-French L A and Couper D (2003). Electromagnetic fields, polychlorinated biphenyls, and prostate cancer mortality in electric utility workers. *Am J Epidemiol,* **157**, 683–91.

Charny C K, Hagmann M J and Levin R L (1987). A whole body thermal model of man during hyperthermia. *IEEE Trans Biomed Eng,* **34**, 375–86.

Chatterjee I, Wu D and Gandhi O P (1986). Human body impedance and threshold currents for perception and pain for contact hazard analysis in the VLF-MF band. *IEEE Trans Biomed Eng,* **33**, 486–94.

Cheever K L, Swearengin T F, Edwards R M, Nelson B K, Werren D W, Conover D L and DeBord D G (2001). 2-methoxyethanol metabolism, embryonic distribution, and macromolecular adduct formation in the rat: the effect of radiofrequency radiation-induced hyperthermia. *Toxicol Lett,* **122**, 53–67.

Chen J-Y and Gandhi O P (1989). RF currents induced in an anatomically based human model of a human for plane wave exposures (20–100 MHz). *Health Phys,* **57**, 89–98.

Chen M M and Holmes K R (1980). Microvascular contributions in tissue heat transfer. *Ann NY Acad Sci,* **335**, 137–50.

Chew S, Ahmadi A, Goh P S and Foong L C (2001). The effects of 1.5 T magnetic resonance imaging on early murine *in-vitro* embryo development. *J Magn Reson Imaging,* **13**(3), 417–20.

Chia S-E, Chia H-P and Tan J-S (2000). Prevalence of headaches among handheld cellular phone users in Singapore: a community study. *Environ Health Perspect,* **108**(11), 1059–62.

Chignell C F and Sik R H (1998). The effects of static magnetic fields on the photohemolysis of human erthrocytes by ketoprofen. *Photochem Photobiol,* **67**(5), 591–5.

Chizhenkova R A and Safroshkina A A (1996). Electrical reactions of brain to microwave irradiation. *Electro-Magnetobiol,* **15**, 253–8.

Cho YH and Chung HW (2003). The effect of extremely low frequency electromagnetic fields (ELF-EMF) on the frequency of micronuclei and sister chromatid exchange in human lymphocytes induced by benzo(a)pyrene. *Toxicol Lett,* **143**, 37–44.

Chou C-K, Guy A W, Kunz L L, Johnson R B, Crowley J J and Krupp J H (1992). Long-term, low-level microwave irradiation of rats. *Bioelectromagnetics,***13**, 469–96.

Clairmont B A, Johnson G B, Zaffanella L E and Zelingher S (1989). The effects of HVAC-HVDC line separation in a hybrid corridor. *IEEE Trans Power Deliv,* **4**, 1338–50.

Cleary S F, Cao G, Liu L-M, Egle P M and Shelton K R (1997). Stress proteins are not induced in mammalian cells exposed to radiofrequency or microwave radiation. *Bioelectromagnetics,* **18**, 499–505.

Clejan S, Dotson R S, Ide C F and Beckman B S (1995). Coordinated effects of electromagnetic field exposure on erythropoietin-induced activities of phosphatidylinositol-phospholipase C and phosphatidylinositol 3-kinase. *Cell Biochem Biophys,* **27**(3), 203–25.

Cobb B L, Jauchem J R, Mason P A, Dooley M P, Miller S A, Ziriax J M and Murphy M R (2000). Neural and behavioral teratological evaluation of rats exposed to ultra-wideband electromagnetic fields. *Bioelectromagnetics,* **21**, 524–37.

Cobb B L, Jauchem J R and Adair E R (2004). Radial arm maze performance of rats following repeated low level microwave radiation exposure. *Bioelectromagnetics,* **25**, 49–57.

Coelho A M Jr, Easley J P, Rogers W R (1991). Effects of exposure to 30 kV/m eletric fields on the social behaviour of baboons. *Bioelectromagnetics,* **12**(2), 117–23.

Coelho A M Jr, Rogers W R and Easley J P (1995). Effects of concurrent exposure to 60 Hz electric and magnetic fields on the social behaviour of baboons. *Bioelectromagnetics,* **Suppl 3**, 71–92.

Cook C M, Thomas A W and Prato F S (2002). Human electrophysiological and cognitive effects of exposure to ELF magnetic and ELF modulated RF and microwave fields: a review of recent studies. *Bioelectromagnetics,* **23**, 144–57.

Cook M R, Graham C, Cohen H D and Gerkovich M M (1992). A replication study of human exposure to 60 Hz fields: effects on neurobehavioral measures. *Bioelectromagnetics,* **13**(4), 261–85.

Cooke P and Morris P G (1981). The effects of exposure on living organisms. II. A genetic study of human lymphocytes. *Br J Radiol,* **54**, 622.

Cooper P J, Garny A and Kohl P (2003). Cardiac electrophysiology: theoretical considerations on a potential target for weak electromagnetic field effects. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 363–8.

Corti R, Fuster V, Badimon J J, Hutter R and Fayad Z A (2001). New understanding of atherosclerosis (clinically and experimentally) with evolving MRI technology *in vivo*. *Ann NY Acad Sci,* **947**, 181–98.

CO-SUR (2002). Risk: improving government's capability to handle risk and uncertainty. Cabinet Office Strategy Unit Report – November 2002, London. http://www.strategy.gov.uk/2002/risk/risk/home.html.

Coulton L A and Barker A T (1993). Magnetic fields and intracellular calcium: effects on lymphocytes exposed to conditions for 'cyclotron resonance'. *Phys Med Biol,* **38**(3), 347–60.

Cox C F, Brewer LJ, Raema C H, Schryver C A, Child S Z and Carstensen E L (1993). A test for teratological effects of power frequency magnetic fields on chick embryos. *IEEE Trans Biomed Eng,* **40**(7), 605–10.

Cranfield C G, Wood A W, Anderson V and Menezes K G (2001). Effects of mobile phone type signals on calcium levels within human leukaemic T-cells (Jurkat cells). *Int J Radiat Biol,* **77**, 1207–17.

Crasson M, Legros J J, Scarpa P and Legros W (1999). 50 Hz magnetic field exposure influence on human performance and psychophysiological parameters: two double-blind experimental studies. *Bioelectromagnetics,* **20**(8), 474–86.

Crasson M, Beckers V, Pequeux Ch, Claustrat B and Legros J J (2001). Daytime 50 Hz magnetic field exposure and plasma melatonin and urinary 6-sulfatoxymelatonin concentration profiles in humans. *J Pineal Res,* **31**, 234–41.

Creim J A, Lovely R H, Kaune W T and Phillips R D (1984). Attempts to produce taste-aversion learning in rats exposed to 60 Hz electric fields. *Bioelectromagnetics,* **5**(2), 271–82.

Creim J A, Lovely R H, Weigel R J, Forsythe W C and Anderson L E (1993). Rats avoid exposure to HVdc electric fields: a dose response study. *Bioelectromagnetics,* **14**, 341–52.

Creim J A, Lovely R H, Weigel R J, Forsythe W C and Anderson L E (1995). Failure to produce taste-aversion learning in rats exposed to static electric fields and air ions. *Bioelectromagnetics,* **16**(5), 301–6.

Cress L W, Owen R D and Desta A B (1999). Ornithine decarboxylase activity in L929 cells following exposure to 60 Hz magnetic fields. *Carcinogenesis,* **20**(6), 1025–30.

Cridland N A, Sienkiewicz Z J, Kowalczuk C I and Saunders R D (1996a). Recent biological studies relevant to carcinogenesis. IN *Biological Effects of Magnetic and Electromagnetic Fields* (S Ueno, ed). New York, Plenum Press, pp 221–38.

Cridland N A, Cragg T A, Haylock R G and Saunders R D (1996b). Effects of 50 Hz magnetic field exposure on the rate of DNA synthesis by normal human fibroblasts. *Int J Radiat Biol,* **69**(4), 503–11.

Cridland N A, Haylock R G and Saunders R D (1999). 50 Hz magnetic field exposure alters onset of S-phase in normal human fibroblasts. *Bioelectromagnetics,* **20**(7), 446–52.

Croft R J, Chandler J S, Burgess A P, Barry R J, Williams J D and Clarke A R (2002). Acute mobile phone operation affects neural function in humans. *Clin Neurophysiol,* **113**, 1623–32.

CST (1994). The MAFIA collaboration. Users guide MAFIA version 3.x. CST GmbH, Lautenschlaegerstr 38 D 64289, Darmstadt.

Curriero F C, Heiner K S, Samet J M, Zeger S L, Strug L and Patz J A (2002). Temperature and mortality in 11 cities of the eastern United States. *Am J Epidemiol,* **155**, 80–87.

D'Ambrosio G, Massa R, Scarfi M R and Zeni O (2002). Cytogenetic damage in human lymphocytes following GMSK phase modulated microwave exposure. *Bioelectromagnetics,* **23**(1), 7–13.

D'Andrea J A (1999). Behavioral evaluation of microwave irradiation. *Bioelectromagnetics,* **20**, 64–74.

D'Andrea J A, Adair E R and de Lorge J O (2003a). Behavioral and cognitive effects of microwave exposure. *Bioelectromagnetics,* **Suppl 6**, S39–62.

D'Andrea J A, Chou C K, Johnston S A and Adair E R (2003b). Microwave effects on the nervous system. *Bioelectromagnetics,* **Suppl 6**, S107–47.

Dahl O, Dalene R, Schem B C and Mella O (1999). Status of clinical hyperthermia. *Acta Oncol,* **38**(7), 863–73.

Daniells C, Duce I, Thomas D, Sewell P, Tattersall J and de Pomerai D (1998). Transgenic nematodes as biomonitors of microwave-induced stress. *Mutat Res,* **399**, 55–64.

Davis H P, Mizumori S Y J, Allen H, Rosenzweig M R, Bennett E L and Tenforde T S (1984). Behavioral studies with mice exposed to DC and 60 Hz magnetic fields. *Bioelectromagnetics,* **5**, 147.

Davis S, Kaune W T, Mirick D K, Chen C and Stevens R G (2001). Residential magnetic fields, light-at-night, and nocturnal urinary 6-sulfatoxymelatonin concentration in women. *Am J Epidemiol,* **154**, 591–600.

Davis S, Mirick D K and Stevens R G (2002). Residential magnetic fields and the risk of breast cancer. *Am J Epidemiol,* **155**, 446–54.

Dawson T W and Stuchly M A (1997). A comparison of analytical and numerical solutions for induction in a sphere with equatorially varying conductivity by low-frequency uniform magnetic fields of arbitrary orientation. IN Proceedings 1997 Symposium of the Applied Computational Electromagnetics Society, pp 533–40.

Dawson T W and Stuchly M A (1998). High resolution organ dosimetry for human exposure to low-frequency magnetic fields. *IEEE Trans Magn,* **34**(3), 708–18.

Dawson T W, De Moerloose J and Stuchly M A (1996). Comparison of magnetically induced ELF fields in humans computed by FDTD and scalar potential FD codes. *ACES J,* **11**(3), 63–71.

Dawson T W, Caputa K and Stuchly M A (1997). Influence of human model resolution on computed currents induced in organs by 60 Hz magnetic fields. *Bioelectromagnetics,* **18**(7), 478–90.

Dawson T W, Caputa K and Stuchly M A (1998). High resolution organ dosimetry for human exposure to low-frequency electric fields. *IEEE Trans Power Deliv,* **13**(2), 366–73.

Dawson T W, Caputa K and Stuchly M A (1999). Numerical evaluation of 60 Hz magnetic induction in the human body in complex occupational environments. *Phys Med Biol,* **44**, 1025–40.

Dawson T W, Potter M and Stuchly M A (2001). Accuracy evaluation of modeling of low frequency field interactions with the human body. *ACES J,* **16**(2) 162–72.

de Lorge J (1979). Effects of magnetic fields on behaviour in nonhuman primates. IN *Magnetic Field Effects on Biological Systems* (T S Tenforde, ed). London, Plenum Press, p 37.

de Lorge J O (1983). The thermal basis for disruption of operant behaviour by microwaves in three animal species. IN *Microwaves and Thermoregulation* (E R Adair, ed). New York, Academic Press.

de Moerloose J, Dawson T W and Stuchly M A (1997). Application of FDTD to quasi-static field analysis. *Radio Sci,* **32** (2), 329–41.

de Pomerai D I, Mutwakil M H A Z, Henshaw J and Emerson L (1999). Mobile phone effects on nematode worms: animal *in vivo* studies using *Caenorhabditis elegans*. IN *Mobile Telephones and Health: An Update of the Latest Research,* Conference Proceedings, Gothenburg, September 1999. City and Financial, Old Woking, pp 67–78.

de Pomerai D, Daniells C, David H, Allan J, Duce I, Mutwakil M, Thomas D, Sewell P, Tattersall J, Jones D and Candido P (2000a). Non-thermal heat-shock response to microwaves. *Nature,* **405** (6785), 417–18.

de Pomerai D, Daniells C, David H, Allan J, Duce I, Mutwakil M, Thomas D, Sewell P, Tattersall J, Jones D and Candido P (2000b). Microwave radiation induces a heat-shock response and enhances growth in the nematode *Caenorhabditis elegans. IEEE Trans Microwave Theory Techniq,* **48**, 2076–81.

de Pomerai D I, Dawe A, Djerdid L, Allan J, Brunt G and Daniells C (2002). Growth and maturation of the nematode *Caenorhabditis elegans* following exposure to weak microwave fields. *Enzyme Microb Techniq,* **30**, 73–9.

De Sanctis J T (2001). Percutaneous interventions for lower extremity peripheral vascular disease. *Am Fam Physician,* **64**(12), 1965–72.

De Vita R, Cavallo D, Raganella L, Eleuteri P, Grollino M G and Calugi A (1995). Effects of 50 Hz magnetic fields on mouse spermatogenesis monitored by flow cytometric analysis. *Bioelectromagnetics,* **16**(5), 330–34.

Dees C, Garrett S, Henley D and Travis C (1996). Effects of 60 Hz fields, estradiol and xenoestrogens on human breast cancer cells. *Radiat Res,* **146**(4), 444–52.

Desjobert H, Hillion J, Adolphe M, Averlant G and Nafziger J (1995). Effects of 50 Hz magnetic fields on C-myc transcript levels in nonsynchronized and synchronized human cells. *Bioelectromagnetics,* **16**(5), 277–83.

Devary L, Brugere H, Debray M, Bernard M, Pupin F, Patinot C, Jacquemont C, Guillosson J J and Nafziger J (2000). Can 50 Hz magnetic fields alter iron metabolism and induce anaemia? *Int J Radiat Biol,* **76**(12), 1669–76.

Dewhirst M W, Lora-Michiels M and Vigilianti B J, Dewey W C, Repacholi M (2003). Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. *Int J Hyperthermia,* **19**(3), 267–94.

Dibirdik I, Kristupaitis D, Kurosaki T, Tuel-Ahlgren L, Chu A, Pond D, Tuong D, Luben R and Uckun F M (1998). Stimulation of Src family protein-tyrosine kinases as a proximal and mandatory step for SYK kinase-dependent phospholipase Cgamma2 activation in lymphoma B cells exposed to low energy electromagnetic fields. *J Biol Chem,* **273**(7), 4035–9.

DiGiovanni J, Johnston D A, Rupp T, Sasser L B, Anderson L E, Morris J E, Miller D L, Kavet R and Walborg E F Jr (1999). Lack of effect of a 60 Hz magnetic field on biomarkers of tumor promotion in the skin of SENCAR mice. *Carcinogenesis,* **20**(4), 685–9.

Dimbylow P J (1996). The development of realistic voxel phantoms for electromagnetic field dosimetry. IN Proceedings International Workshop on Voxel Phantom Development. Chilton, NRPB, pp 1–7.

Dimbylow P J (1997a). FDTD calculations of the whole body averaged SAR in an anatomically realistic voxel model of the human body from 1 MHz to 1 GHz. *Phys Med Biol,* **42** 479–90.

Dimbylow P J (1997b). The calculation of localised SAR in a 2 mm resolution anatomically realistic model of the lower leg. *Radiat Prot Dosim,* **72**(3–4), 321–6.

Dimbylow P J (1998). Induced current densities from low-frequency magnetic fields in a 2 mm resolution, anatomically realistic model of the body. *Phys Med Biol,* **43** 221–30.

Dimbylow P J (2000). Current densities in a 2 mm resolution anatomically realistic model of the body induced by low-frequency electric fields. *Phys Med Biol,* **45** 1013–22.

Dimbylow P J (2001). The relationship between localised SAR in the arm and wrist current. *Radiat Prot Dosim,* **95**(2), 177–9.

Dimbylow P J (2002). Fine resolution calculations of SAR in the human body for frequencies up to 3 GHz. *Phys Med Biol,* **47**, 2835–46.

Dimbylow P J and Mann S M (1994). SAR calculations in an anatomically based realistic model of the head for mobile transceivers at 900 MHz and 1.8 GHz. *Phys Med Biol,* **39** 1537–53.

Dolk H, Elliott P, Shaddick G, Walls P and Thakrar B (1997). Cancer incidence near radio and television transmitters in Great Britain. II. All high power transmitters. *Am J Epidemiol,* **145**, 10–17.

Doll R (1998). Epidemiological evidence of the effects of behaviour and the environment on the risk of human cancer. *Recent Res Cancer Res,* **154**, 3–21.

Donaldson G C, Keatinge W R and Saunders R D (2003). Cardiovascular responses to heat stress and their adverse consequences in healthy and vulnerable human populations. IN Proceedings WHO Workshop on Adverse Temperature Levels in the Human Body, Geneva, March 2002. *Int J Hyperthermia,* **19**(3), 225–35.

Donaldson G C, Kovats R S, Keatinge W R and McMichael R J (2001). The potential impact of climate change on heat- and cold-related mortality and morbidity. IN *Health Effects of Climate Change in the UK* (R Maynard and E Green, eds). Report to the Department of Health (UK), Chapter 3.1.1.

Dowling J E (1987). *The Retina: An Approachable Part of the Brain.* Cambridge, Harvard University Press.

Dubreuil D, Jay T M and Edeline J-M (2002). Does head-only exposure to GSM-900 MHz electromagnetic fields affect the performance of rats in spatial learning task? *Behav Brain Res,* **129**, 203–10.

Dubreuil D, Jay T M and Edeline J-M (2003). Head-only exposure to GSM-900 MHz electromagnetic fields does not alter rat's memeory in spatial and non-spatial tasks. *Behav Brain Res,* **145**, 51–61.

Durand D (2003). Electric field effects in hyperexcitable tissue: a review. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 325–32.

Easley S P, Coelho A M Jr and Rogers W R (1991). Effects of exposure to a 60-kV/m, 60 Hz electric field on the social behavior of baboons. *Bioelectromagnetics,* **12**(6), 361–75.

EC (2000). Commission of the European Communities. Communication from the Commission on the precautionary principle. COM(2000) 1. Luxembourg, EC. http://europa.eu.int/comm/dgs/health_consumer/library/pub/pub07_en.pdf.

Edelstyn N and Oldershaw A (2002). The acute effects of exposure to the electromagnetic field emitted by mobile phones on human attention. *Neuroreport,* **13**(1), 119–21.

Edwards M J, Shiota K, Smith M S R and Walsh D A (1995). Hyperthermia and birth defects. *Reprod Toxicol,* **9**, 411–25.

Edwards M J, Saunders R D and Shiota K (2003). Effects of heat on embryos and foetuses. *Int J Hyperthermia,* **19**(3), 295–324.

Edwards N A (1986). The estimation of currents in the head induced by power frequency electric fields: Mathematics as an aid to experiment. Leatherhead, Surrey, Central Electricity Generating Board, Central Electricity Research Laboratories, CEGB/TPRD/L/3002/R86.

Edwards N A and Pickles J H (1985). Mathematics as an aid to experiment: human body currents induced by power frequency electric fields. IN International Conference on Electric and Magnetic Fields in Medicine and Biology. London, December 1985. London, Institution of Electrical Engineers, Conference Publication No 257, 98–102.

Ekstrom T, Mild K H and Holmberg B (1998). Mammary tumours in Sprague-Dawley rats after initiation with DMBA followed by exposure to 50 Hz electromagnetic fields in a promotional scheme. *Cancer Lett,* **123**(1), 107–11.

Elbetieha A, Al-Akhras M A and Darmani H (2002). Long-term exposure of male and female mice to 50 Hz magnetic field: effects on fertility. *Bioelectromagnetics,* **23**(2), 168–72.

Elder J A (2003a). Survival and cancer in laboratory mammals exposed to radiofrequency energy. *Bioelectromagnetics,* **Suppl 6**, S101–6.

Elder J A (2003b). Ocular effects of radiofrequency energy. *Bioelectromagnetics,* **Suppl 6**, S148–61.

Elder J A and Chou C K (2003). Auditory response to pulsed radiofrequency energy. *Bioelectromagnetics,* **Suppl 6**, S162–73.

Elwood J M (1999). A critical review of epidemiologic studies of radiofrequency exposure and human cancers. *Environ Health Perspect,* **107**(Suppl 1), 155–68.

Engelborghs S, D'Hooge R and De Deyn P P (2000). Pathophysiology of epilepsy. *Acta Neurol Belg,* **100**, 201–13.

Erkkola R U, Pirhonen J P and Kivijarvi A K (1992). Flow velocity waveforms in uterine and umbilical arteries during submaximal bicycle exercise in normal pregnancy. *Obstet Gynaecol,* **79**, 611–15.

Erren T C (2001). A meta-analysis of epidemiologic studies of electric and magnetic fields and breast cancer in women and men. *Bioelectromagnetics,* **Suppl 5**, S105–19.

Erren T C (2002). Does light cause internal cancers? The problem and challenge of an ubiquitous exposure. *Neuroendcrinol Lett,* **23**, 61–70.

Espinar A, Piera V, Carmona A and Guerrero J M (1997). Histological changes during development of the cerebellum in the chick embryo exposed to a static magnetic field. *Bioelectromagnetics,* **18**(1), 36–46.

Eulitz C, Ullsperger P, Freude G and Elbert T (1998). Mobile phones modulate response patterns of human brain activity. *Neuroreport,* **9**(14), 3229–32.

Fairbairn D W and O'Neill K L (1994). The effect of electromagnetic field exposure on the formation of DNA single strand breaks in human cells. *Cell Mol Biol (Noisy-le-grand),* **40**(4), 561–7.

Falk B (1998). Effects of thermal stress during rest and exercise in the paediatric population. *Sports Med,* **25**(4), 221–40.

Falk M H and Issels R D (2001). Hyperthermia in oncology. *Int J Hyperthermia,* **17**(1), 1–18.

Fam W Z (1981). Prolonged exposure of mice to 340 kV m^{-1} electrostatic field. *IEEE Trans Biomed Eng,* **28**, 453.

Fam W Z and Mikhail E L (1996). Lymphoma induced in mice chronically exposed to very strong low-frequency electromagnetic field. *Cancer Lett,* **105**(2), 257–69.

Fanelli C, Coppola S, Barone R, Colussi C, Gualandi G, Volpe P and Ghibelli L (1996). Magnetic fields increase cell survival by inhibiting apoptosis via modulation of Ca^{2+} influx. *FASEB J,* **13**(1), 95–102.

Farrell J M, Litovitz T L, Penafiel M, Montrose C J, Doinov P, Barber M, Brown K M and Litovitz T A (1997). The effect of pulsed and sinusoidal magnetic fields on the morphology of developing chick embryos. *Bioelectromagnetics,* **18**(6), 431–8.

Fedrowitz M, Westermann J and Löscher W (2002). Magnetic field exposure increases cell proliferation but does not affect melatonin levels in the mammary gland of female Sprague Dawley rats. *Cancer Res,* **62**, 1356–63.

Ferrari A U (2002). Modifications of the cardiovascular system with ageing. *Am J Geriatric Cardiol,* **11**(1), 30–39.

Fesenko E E, Makar V R, Novoselova E G and Sadovnikov V B (1999). Microwaves and cellular immunity. I. Effect of whole body microwave irradiation on tumor necrosis factor production in mouse cells. *Bioelectrochem Bioenerg,* **49**(1), 29–35.

Feychting M, Jonsson F, Pedersen N L and Ahlbom A (2003). Occupational magnetic field exposure and neurodegenerative disease. *Epidemiology,* **14**, 413–19; discussion 427–8.

Finnie J W, Blumbergs P C, Manavis J, Utteridge T D, Gebski V, Swift J G, Vernon-Roberts B and Kuchel T R (2001). Effect of global system for mobile communication (GSM)-like radiofrequency fields on vascular permeability in mouse brain. *Pathology,* **33**, 338–40.

Finnie J W, Blumbergs P C, Manavis J, Utteridge T D, Gebski V, Davies R A, Vernon-Roberts B and Kuchel T R (2002). Effect of long-term mobile communication microwave exposure on vascular permeability in mouse brain. *Pathology,* **34**(4), 344–7.

Fiorani M, Cantoni O, Sestili P, Conti R, Nicolini P, Vetrano F and Dacha M (1992). Electric and/or magnetic field effects on DNA structure and function in cultured human cells. *Mutat Res,* **282**(1), 25–9.

Fitzpatrick S M and Rothman D L (2000). Meeting report: transcranial magnetic stimulation and studies of human cognition. *J Cogn Neurosci,* **12**(4), 704–9.

Fitzsimmons R J, Strong D D, Mohan S and Baylink D J (1992). Low-amplitude, low-frequency electric field-stimulated bone cell proliferation may in part be mediated by increased IGF-II release. *J Cell Physiol,* **150**(1), 84–9.

Fleming P J, Gilbert R, Azaz Y, Berry P J, Rudd P T, Stewart A and Hall E (1990). Interaction between bedding and sleeping position in the sudden infant death syndrome: a population based case–control study. *Br Med J,* **301**, 85–9.

Fleming P J, Azaz Y and Wingfield R (1992). Development of thermoregulation in infancy: possible implications for SIDs. *J Clin Pathol,* **45**, 17–19.

Flipo D, Fournier M, Benquet C, Roux P, Le Boulaire C, Pinsky C, LaBella F S and Krzystyniak K (1998). Increased apoptosis, changes in intracellular Ca^{2+}, and functional alterations in lymphocytes and macrophages after *in vitro* exposure to static magnetic field. *J Toxicol Environ Health A,* **54**(1), 63–76.

Flodin U, Seneby A and Tegenfeldt C (2000). Provocation of electric hypersensitivity under everyday conditions. *Scand J Work Environ Health,* **26**(2), 93–8.

Foster K R (2002). The precautionary principle – common sense or environmental extremism? *IEEE Technology and Society Magazine,* Winter 2002/2003, Catalogue Reference 0278-0079/02.

Foster K R and Erdreich L S (1999). Thermal models for microwave hazards and their role in standards development. *Bioelectromagnetics,* **20**, 52–63.

Foster K R, Lozano-Nieto A, Riu P J and Ely T S (1998). Heating of tissues by microwaves: a model analysis. *Bioelectromagnetics,* **19**, 420–28.

Francis J T, Gluckman B J and Schiff S J (2003). Sensitivity of neurons to weak electric fields. *J Neurosci,* **23**(19), 7255–61.

Frei M R, Jauchem J R, Dusch, S J, Merritt J H, Berger R E and Stedham M A (1998a). Chronic, low-level (1.0 W/kg) exposure of mice prone to mammary cancer to 2450 MHz microwaves. *Radiat Res,* **150**, 568–76.

Frei M R, Berger R E, Dusch, S J, Guel V, Jauchem J R, Merritt J H and Stedham M A (1998b). Chronic exposure of cancer-prone mice to low-level 2450 MHz radiofrequency radiation. *Bioelectromagnetics,* **19**, 20–31.

French P W, Penny R, Laurence J A and McKenzie D R (2001). Mobile phones, heat shock proteins and cancer. *Differentiation,* **67**, 93–7.

Freude G, Ullsperger P, Eggert S and Ruppe I (1998). Effects of microwaves emitted by cellular phones on human slow brain potentials. *Bioelectromagnetics,* **19**(6), 384–7.

Freude G, Ullsperger P, Eggert S and Ruppe I (2000). Microwaves emitted by cellular telephones affect human slow brain potentials. *Eur J Appl Physiol,* **81**(1–2),18–27.

Frey A H (1998). Headaches from cellular telephones: are they real and what are the implications? *Environ Health Perspect,* **106**(3), 101–3.

Fritze K, Wiessner C, Kuster N, Sommer C, Gass P, Hermann D M, Kiessling M and Hossmann K-A (1997a). Effect of global system for mobile communication microwave exposure on the genomic response of the rat brain. *Neuroscience,* **81**, 627–39.

Fritze K, Sommer C, Schmitz B, Mies G, Hossmann K A, Kiessling M and Wiessner C (1997b). Effect of global system for mobile communication (GSM) microwave exposure on blood–brain barrier permeability in rat. *Acta Neuropathol (Berl),* **94**, 465–70.

Fujiwara O, Yano M and Wang J (1999). FDTD computation of temperature rise inside a realistic head model for 1.5 GHz microwave exposure. *Electronics and Communications in Japan,* Part 1 (Communications), **82**, 11–19.

Furse C M and Gandhi O P (1998). Calculation of electric fields and currents induced in a millimeter-resolution human model at 60 Hz using the FDTD method. *Bioelectromagnetics,* **19**, 293–9.

Gabriel C (1995). Compilation of the dielectric properties of body tissues at RF and microwave frequencies. Report prepared for NRPB by Microwave Consultants Ltd.

Gabriel C (1996). Compilation of the dielectric properties of body tissues at RF and microwave frequencies. US Air Force Armstrong Laboratory, Technical Report AL/OE-TR-1996-0037.

Gabriel C, Gabriel S and Corthout E (1996a). The dielectric properties of biological tissues: 1. Literature survey. *Phys Med Biol,* **41**, 2231–49.

Gabriel S, Lau R W and Gabriel C (1996b). The dielectric properties of biological tissues: 2. Measurements in the frequency range 10 Hz to 20 GHz. *Phys Med Biol,* **41**, 2251–69.

Gabriel S, Lau R W and Gabriel C (1996c). The dielectric properties of biological tissues: 3. Parametric models for the dielectric spectrum of tissues. *Phys Med Biol,* **41**, 2271–93.

Gaffey C T and Tenforde T S (1979). Changes in the electrocardiograms of rats and dogs exposed to DC magnetic fields. Berkeley CA, University of California, Lawrence Berkeley Laboratory, LBL-9085.

Gaffey C T and Tenforde T S (1981). Alterations in the rat electrocardiogram induced by stationary magnetic fields. *Bioelectromagnetics,* **1**, 357.

Gaffey C T and Tenforde T S (1983). Bioelectric properties of frog sciatic nerves during exposure to stationary magnetic fields. *Radiat Environ Biophys,* **22**, 61.

Gaffey C T, Tenforde T S and Dean E E (1980). Alterations in the electrocardiograms of baboons exposed to DC magnetic fields. *Bioelectromagnetics,* **1**, 209.

Gajsek P, Hurt W D, Ziriax J M and Mason P A (2001). Parametric dependence of SAR on permittivity values in a man model. *IEEE Trans Biomed Eng,* **48**(10), 1169–76.

Galt S, Wahlstrom J, Hamnerius Y, Holmqvist D and Johannesson T (1995). Study of effects of 50 Hz magnetic fields on chromosome aberrations and the growth-related enzme ODC in human amniotic cells. *Bioelectrochem Bioenerg,* **36**, 1–8.

Galvanovskis J, Sandblom J, Bergqvist B, Galt S and Hamnerius Y (1996). The influence of 50 Hz magnetic fields on cytoplasmic Ca^{2+} oscillations in human leukemia T-cells. *Sci Total Environ,* **180**(1), 19–33.

Gamberale F, Olson B A, Eneroth P, Lindh T and Wennberg A (1989). Acute effects of ELF electromagnetic fields: a field study of linesmen working with 400 kV power lines. *Br J Ind Med,* **46**(10), 729–37.

Gamble S C, Wolff H and Arrand J E (1999). Syrian hamster dermal cell immortalization is not enhanced by power line frequency electromagnetic field exposure. *Br J Cancer,* **81**(3), 377–80.

Gandhi O P and Chen J-Y (1992). Numerical dosimetry at power-line frequencies using anatomically based models. *Bioelectromagnetics,* **Suppl 1**, 43–60.

Gandhi O P and Kang G (2001). Calculation of induced current densities for humans by magnetic fields from electronic surveillance devices. *Phys Med Biol,* **46**, 2759–71.

Gandhi O P, DeFord J F and Kanai, H (1984). Impedance method for calculation of power deposition patterns in magnetically induced hyperthermia. *IEEE Trans Biomed Eng,* **31**, 644–51.

Gandhi O P, Gu Y-G, Chen J-Y and Bassen H (1992). Specific absorption rates and induced current distributions in an anatomically based human model for plane wave exposures. *Health Phys,* **63**, 281–90.

Gandhi O P, Lazzi G and Furse C M (1996). Electromagnetic absorption in the human head and neck for mobile telephones at 835 and 1900 MHz. *IEEE Trans Microwave Theory Techniq,* **44** 1884–97.

Gandhi O P, Kang G, Wu D and Lazzi G (2001a). Currents induced in anatomic models of the human for uniform and nonuniform power frequency magnetic fields. *Bioelectromagnetics,* **22**, 112–21.

Gandhi O P, Li Q-X and Kang G (2001b). Temperature rise for the human head for cellular telephones and for peak SARs prescribed in safety guidelines. *IEEE Trans Microwave Theory Techniq,* **49**, 2126–32.

Gangi S and Johansson O (2000). A theoretical model based upon mast cells and histamine to explain the recently proclaimed sensitivity to electric and/or magnetic fields in humans. *Med Hypotheses,* **54**(4), 663–71.

Geard C R, Osmak R S, Hall E J, Simon H E, Maudaley A A and Hilal S K (1984). Magnetic resonance and ionizing radiation: a comparative evaluation *in vitro* of oncogenic and genotoxic potential. *Radiology,* **152**, 199.

Gluckman B J, Nguyen H, Weinstein S L and Schiff S J (2001). Adaptive electric field control of epileptic seizures. *J Neurosci,* **21**(2), 590–600.

Gmitrov J and Ohkubo C (2002a). Artificial static and geomagnetic field interrelated impact on cardiovascular regulation. *Bioelectromagnetics,* **23**(5), 329–38.

Gmitrov J and Ohkubo C (2002b). Verapamil protective effect on natural and artificial magnetic field cardiovascular impact. *Bioelectromagnetics,* **23**(7), 531–41.

Gmitrov J, Ohkubo C and Okano H (2002). Effect of 0.25 T static magnetic field on microcirculation in rabbits. *Bioelectromagnetics,* **23**(3), 224–9.

Gold S, Goodman R and Shirley-Henderson A (1994). Exposure of simian virus-40-transformed human cells to magnetic fields results in increased levels of T-antigen mRNA and protein. *Bioelectromagnetics,* **15**(4), 329–36.

Goldstein L S, Dewhirst M W, Repacholi M and Kheifets L (2003). Summary, conclusions and recommendations: adverse temperature levels in the human body. *Int J Hyperthermia,* **19**(3), 385–90.

Gona A G, Yu M C, Gona O, Al-Rabiai S, Von Hagen S and Cohen E (1993). Effects of 60 Hz electric and magnetic fields on the development of the rat cerebellum. *Bioelectromagnetics,* **14**(5), 433–47.

Goodman E M, Greenebaum B and Marron M T (1994). Magnetic fields after translation in *Escherichia coli*. *Bioelectromagnetics,* **15**(1), 77–83.

Gordon C J (1984). Thermal physiology. IN *Biological Effects of Radiofrequency Radiation* (J A Elder and D F Cahill, eds). North Carolina, Health Effect Research Laboratory, United States Environmental Protection Agency, EPA-600/8-83-026F, pp 4–12.

Gos P, Eicher B, Kohli J and Heyer W D (1997). Extremely high frequency electromagnetic fields at low power density do not affect the division of exponential phase *Saccharomyces cerevisiae* cells. *Bioelectromagnetics,* **18**, 142–55.

Gos P, Eicher B, Kohli J and Heyer W D (2000). No mutagenic or recombinogenic effects of mobile phone fields at 900 MHz detected in the yeast *Saccharomyces cerevisiae*. *Bioelectromagnetics,* **21**, 515–23.

Goswami P C, Albee L D, Parsian A J, Baty J D, Moros E G, Pickard W F, Roti Roti J L and Hunt C R (1999). Proto-oncogene mRNA levels and activities of multiple transcription factors in C3H 10T1/2 murine embryonic fibroblasts exposed to 835.62 and 847.74 MHz cellular phone communication frequency radiation. *Radiat Res,* **151**, 300–309.

Graham C and Cook M R (1999). Human sleep in 60 Hz magnetic fields. *Bioelectromagnetics,* **20**(5), 277–83.

Graham C, Cook M R and Cohen H D (1990). Final report: immunological and biochemical effects of 60 Hz electric and magnetic fields in humans. Springfield VA, National Technical Information Service, Report DE90006671.

Graham C, Cook M R, Cohen H D and Gerkovich M M (1994). Dose response study of human exposure to 60 Hz electric and magnetic fields. *Bioelectromagnetics,* **15**(5), 447–63.

Graham C, Cook M R, Riffle D W, Gerkovich M M and Cohen H D (1996). Nocturnal melatonin levels in human volunteers exposed to intermittent 60 Hz magnetic fields. *Bioelectromagnetics,* **17**(4), 263–73.

Graham C, Cook M R and Riffle D W (1997). Human melatonin during continuous magnetic field exposure. *Bioelectromagnetics,* **18**(2), 166–71.

Graham C, Cook M R, Cohen H D, Riffle D W, Hoffman S and Gerkovich M M (1999). Human exposure to 60 Hz magnetic fields: neurophysiological effects. *Int J Psychophysiol,* **33**(2), 169–75.

Graham C, Cook M R, Sastre A, Riffle D W and Gerkovich M M (2000a). Multi-night exposure to 60 Hz magnetic fields: effects on melatonin and its enzymatic metabolite. *J Pineal Res,* **28**(1), 1–8.

Graham C, Sastre A, Cook M R and Gerkovich M M (2000b). Nocturnal magnetic field exposure: gender-specific effects on heart rate variability and sleep. *Clin Neurophysiol,* **111**(11), 1936–41.

Graham C, Sastre A, Cook M R and Kavet R (2000c). Heart rate variability and physiological arousal in men exposed to 60 Hz magnetic fields. *Bioelectromagnetics,* **21**(6), 480–82.

Graham C, Sastre A, Cook M R, Kavet R, Gerkovitch M M and Riffle D (2000d). Exposure to strong ELF magnetic fields does not alter cardiac autonomic control mechanisms. *Bioelectromagnetics,* **21**, 413–21.

Graham C, Cook M R, Sastre A, Gerkovich M M and Kavet R (2000e). Cardiac autonomic control mechanisms in power-frequency magnetic fields: a multistudy analysis. *Environ Health Perspect,* **108**(8), 737–42.

Graham C, Cook M R, Gerkovich M M and Sastre A (2001a). Melatonin and 6-OHMS in high-intensity magnetic fields. *J Pineal Res,* **31**, 85–8.

Graham C, Sastre A, Cook M R and Gerkovich M M (2001b). All-night exposure to EMF does not alter urinary melatonin 6-OHMS or immune measures in older men and women. *J Pineal Res,* **31**, 109–13.

Graham J H, Fletcher D, Tigue J and McDonald M (2000). Growth and developmental stability of *Drosophila melanogaster* in low frequency magnetic fields. *Bioelectromagnetics,* **21**(6), 465–72.

Graham J M, Edwards M J and Edwards M J (1998). Teratogen update: gestational effects of maternal hyperthermia due to febrile illnesses and resultant patterns of defects in humans. *Teratology,* **58**, 209–21.

Greaves M (2002). Childhood leukaemia. *Br Med J,* **324**, 283–7.

Greene J J, Pearson S L, Skowronski W J, Nardone R M, Mullins J M and Krause D (1993). Gene-specific modulation of RNA synthesis and degradation by extremely low frequency electromagnetic fields. *Cell Mol Biol (Noisy-le-grand),* **39**(3), 261–8.

Griefahn B, Kunemund C, Blaszkewicz M, Lerchl A and Degen G H (2002). Effects of electromagnetic radiation (bright light, extremely low-frequency magnetic fields, infrared radiation) on the circadian rhythm of melatonin synthesis, rectal temperature and heart rate. *Ind Health,* **40**, 320–27.

Grissom C B (1995). Magnetic field effects in biology: a survey of possible mechanisms with emphasis on radical-pair recombination. *Chem Rev,* **95**, 3–24.

Grota L J, Reiter R J, Keng P, Michaelson S (1994). Electric field exposure alters serum melatonin but not pineal melatonin synthesis in male rats. *Bioelectromagnetics,* **15**(5), 427–37.

Groves F D, Page W F, Gridley G, Lisimaque L, Stewart P A, Tarone R E, Gail M H, Boice J D Jr and Beebe G W (2002). Cancer in Korean war navy technicians: mortality survey after 40 years. *Am J Epidemiol,* **155**, 810–18.

Guy A W, Lin J C, Kramar P O and Emery A (1975). Effect of 2450 MHz radiation on the rabbit eye. *IEEE Trans Microwave Theory Techniq,* **23**, 492–8.

Haarala C, Bjornberg L, Ek M, Laine M, Revonsuo A, Koivisto M and Hamalainen H (2003). Effect of a 902 MHz electromagnetic field emitted by mobile phones on human cognitive function: a replication study. *Bioelectromagnetics,* **24**(4), 283–8.

Håkansson N, Floderus B, Gustavsson P, Johansen C and Olsen J H (2002). Cancer incidence and magnetic field exposure in industries using resistance welding in Sweden. *Occup Environ Med,* **59**, 481–6.

Håkansson N, Gustavsson P, Johansen C and Floderus B (2003a). Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields. *Epidemiology,* **14**, 420–26; discussion 427–8.

Håkansson N, Gustavsson P, Sastre A and Floderus B (2003b). Occupational exposure to extremely low frequency magnetic fields and mortality from cardiovascular disease. *Am J Epidemiol,* **158**, 534–42.

Hallberg O and Johansson O (2002). Melanoma incidence and frequency modulation (FM) broadcasting. *Arch Environ Health,* **57**, 32–40.

Hamblin D L and Wood A W (2002). Effects of mobile phone emissions on human brain activity and sleep variables. *Int J Radiat Biol,* **78**(8), 659–69.

Hancock P A (1981). Heat stress impairment of mental performance: a revision of tolerance limits. *Aviat, Space Environ Med,* **52**, 778–84.

Hancock P A (1982). Task categorization and the limits of human performance in extreme heat. *Aviat, Space Environ Med,* **53**, 177–80.

Hancock P A and Meshkati N (eds) (1988). *Human Mental Workload.* Amsterdam, North Holland.

Hancock P A and Vasmatzidis I (1998). Human occupational and performance limits under stress: the thermal environment as a prototypical example. *Ergonomics,* **41**, 1169–91.

Hancock P A and Vasmatzidis I (2000). On the behavioral basis for stress exposure limits: the foundational case of thermal stress. IN *The Occupational Ergonomics Handbook* (W Karwowski and W S Marras, eds). Boca Raton, CRC Press, pp 1707–39.

Hancock P A and Vasmatzidis I (2003). Effects of heat stress on cognitive performance: the current state of knowledge. *Int J Hyperthermia,* **19**(3), 355–72.

Hardell L, Hallquist A, Mild K H, Carlberg M, Pahlson A and Lilja A (2002). Cellular and cordless telephones and the risk for brain tumours. *Eur J Cancer Prev,* **11**(4), 377–86.

Hardell L, Mild K H and Carlberg M (2003). Further aspects on cellular and cordless telephones and brain tumours. *Int J Oncol,* **22**(2), 399–407.

Harland J D and Liburdy R P (1997). Environmental magnetic fields inhibit the antiproliferative action of tamoxifen and melatonin in a human breast cancer cell line. *Bioelectromagnetics,* **18**(8), 555–62.

Harland J D, Levine G A and Liburdy R P (1998). Differential inhibition of tamoxifen's oncostatic functions in a human breast cancer cell line by a 12 mG (1.2 mT) magnetic field. IN *Electricity and Magnetism in Biology and Medicine* (F Bersani, ed). Bologna, Plenum Press.

Harrington J M, Nichols L, Sorahan T and van Tongeren M (2001). Leukaemia mortality in relation to magnetic field exposure: findings from a study of United Kingdom electricity generation and transmission workers. *Occup Environ Med,* **58**, 307–14.

Harris A W, Basten A, Gebski V, Noonan D, Finnie J, Bath M L, Bangay M J and Repacholi M H (1998). A test of lymphoma induction by long-term exposure of E mu-Pim1 transgenic mice to 50 Hz magnetic fields. *Radiat Res,* **149**(3), 300–307.

Harrison G H, Balcer-Kubiczek E K, Shi Z, Zhang Y, McCready W A and Davis C C (1997). Kinetics of gene expression following exposure to 60 Hz, 2 mT magnetic fields in three human cell lines. *Bioelectrochem Bioenerg,* **43**, 1–6.

Haugsdal B, Tynes T, Rotnes J S and Griffiths D (2001). A single nocturnal exposure to 2–7 millitesla static magnetic fields does not inhibit the excretion of 6-sulfatoxymelatonin in healthy young men. *Bioelectromagnetics,* **22**, 1–6.

HCN (1997). Health Council of the Netherlands: Radiofrequency Radiation Committee. Radiofrequency electromagnetic fields (300 Hz – 300 GHz). Rijswijk, Health Council of the Netherlands, Publication Number 1997/01.

HCN (2000). Health Council of the Netherlands. GSM base stations. Rijswijk, Health Council of the Netherlands, Publication Number 2000/16E.

HCN (2002). Health Council of the Netherlands. Mobile telephones; an evaluation of health effects. Rijswijk, Health Council of the Netherlands, Publication Number 2002/01E.

Heikkinen P, Kumlin T, Laitinen J T, Komulainene H and Juutilainen J (1999). Chronic exposure to 50 Hz magnetic fields or 900 MHz electromagnetic fields does not alter nocturnal 6-hydroxymelatonin sulfate secretion in CBA/S mice. *Electro- Magnetobiol,* **18**(1), 33–42.

Heikkinen P, Kosma VM, Huuskonen H, Komulainen H, Kumlin T, Penttila L, Vaananen A, Juutilainen J (2001a). Effects of 50 Hz magnetic fields on cancer induced by ionizing radiation in mice. *Int J Radiat Biol,* **77**, 483–95.

Heikkinen P, Kosma V-M, Hongisto T, Huuskonen, H, Hyysalo P, Komulainen H, Kumlin T, Lahtinen T, Lang S, Puranen L and Juutilainen J (2001b). Effects of mobile phone radiation on x-ray-induced tumorigenesis in mice. *Radiat Res,* **156**, 775–85.

Hermann D M and Hossmann K-A (1997). Neurological effects of microwave exposure related to mobile communication. *J Neurol Sci,* **152**, 1–14.

Heusser K, Tellschaft D and Thoss F (1997). Influence of an alternating 3 Hz magnetic field with an induction of 0.1 millitesla on chosen parameters of the human occipital EEG. *Neurosci Lett,* **239**(2–3), 57–60.

Heynick L N, Johnston S A and Mason P A (2003). Radio frequency electromagnetic fields: cancer, mutagenesis, and genotoxicity. *Bioelectromagnetics,* **Suppl 6**, S74–100.

Heynick L N and Merritt J H (2003). Radiofrequency fields and teratogenesis. *Bioelectromagnetics,* **Suppl 6**, S174–86.

Hietanen M, Kovala T and Hamalainen A M (2000). Human brain activity during exposure to radiofrequency fields emitted by cellular phones. *Scand J Work Environ Health,* **26**(2), 87–92.

Hietanen M, Hamalainen A-M and Husman T (2002). Hypersensitivity symptoms associated with exposure to cellular telephones: no causal link. *Bioelectromagnetics,* **23**(4), 264–70.

Higashi T, Sagawa S, Ashida N and Takeuchi T (1996). Orientation of glutaraldehyde-fixed erythrocytes in strong static magnetic fields. *Bioelectromagnetics,* **17**(4), 335–8.

Higashikubo R, Culbreth V O, Spitz D R, LaRegina M C, Pickard W F, Straube W L, Moros E G and Roti Roti J L (1999). Radiofrequency electromagnetic fields have no effect on the *in vivo* proliferation of the 9L brain tumor. *Radiat Res,* **152**, 665–71.

Higashikubo R, Ragouzis M, Moros E G, Straube W L and Roti Roti J L (2001). Radiofrequency electromagnetic fields do not alter the cell cycle progression of C3H 10T and U87MG cells. *Radiat Res,* **56**, 786–95.

High W B, Sikora J, Ugurbil K and Garwood M (2000). Subchronic *in vivo* effects of a high static magnetic field (9.4 T) in rats. *J Magn Reson Imaging,* **12**(1), 122–39.

Hille B (2001). *Ion Channels of Excitable Membranes* (3rd Edition). Sunderland, Sinauer Associates.

Hillert L, Berglind N, Arnetz B B and Bellander T (2002). Prevalence of self-reported hypersensitivity to electric or magnetic fields in a population-based questionnaire survey. *Scand J Work Environ Health,* **28**(1), 33–41.

Hinsenkamp M, Jercinovic A, de Graef C, Wilaert F and Heenen M (1997). Effects of low frequency pulsed electrical current on keratinocytes *in vitro*. *Bioelectromagnetics,* **18**(3), 250–54.

Hiraoka M, Miyakoshi J, Li Y P, Shung B, Takebe H and Abe M (1992). Induction of c-fos gene expression by exposure to a static magnetic field in HeLaS3 cells. *Cancer Res,* **52**(23), 6522–4.

Hirata A and Shiozawa T (2003). Correlation of maximum temperature increase and peak SAR in the human head due to handset antennas. *IEEE Trans Microwave Theory Techniq,* **51**(7), 1834–41.

Hirata A, Ushio G and Shiozawa T (1999). Formation of hot spots in the human eye for plane wave exposures. IN Proceedings 1999 Asia Pacific Microwave Conference, Singapore, pp 477–80.

Hirata A, Matsuyama S-i and Shiozawa T (2000). Temperature rises in the human eye exposed to EM waves in the frequency range 0.6–6 GHz. *IEEE Trans Electromagn Compat,* **42**, 386–92.

Hirata A, Caputa, Dawson T W and Stuchly M A (2001). Dosimetry in models of child and adult for low-frequency electric field. *IEEE Trans Biomed Eng,* **48**(9), 1007–12.

Hocking B (1998). Preliminary report: symptoms associated with mobile phone use. *Occup Med (Lond),* **48**(6), 357–60.

Hocking B and Joyner K (1992). Health risk management of radio-frequency radiation. *J Occup Health Saf,* **8**, 21–30.

Hocking B and Westerman R (2000). Neurological abnormalities associated with mobile phone use. *Occup Med (Lond),* **50**(5), 366–8.

Hone P, Edwards A, Halls J, Cox R and Lloyd D (2003). Possible associations between ELF electromagnetic fields, DNA damage response processes and childhood leukaemia. *Br J Cancer,* **88**, 1939–41.

Hong S C, Kurokawa Y, Kabuto M and Ohtsuka R (2001). Chronic exposure to ELF magnetic fields during night sleep with eletric sleep: effects on diurnal melatonin rhythms in men. *Bioelectromagnetics,* **22**, 138–43.

House R V and McCormick D L (2000). Modulation of natural killer cell function after exposure to 60 Hz magnetic fields: confirmation of the effect in mature B6C3F1 mice. *Radiat Res,* **153**(5 Part 2), 722–4.

House R V, Ratajczak H V, Gauger J R, Johnson T R, Thomas P T and Mccormick D L (1996). Immune function and host defense in rodents exposed to 60 Hz magnetic fields. *Fundam Appl Toxicol,* **34**(2), 228–39.

Huber R, Graf T, Cote K A, Wittmann L, Gallmann E, Matter D, Schuderer J, Kuster N, Borbely A A and Achermann P (2000). Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG. *Neuroreport,* **11**, 3321–5.

Huber R, Treyer V, Borbely A A, Schuderer J, Gottselig J M, Landolt H P, Werth E, Berthold T, Kuster N, Buck A and Achermann P (2002). Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. *J Sleep Res,* **11**, 289–95.

Huuskonen H, Juutilainen J and Komulainen H (1993). Effects of low-frequency magnetic fields on fetal development in rats. *Bioelectromagnetics,* **14**(3), 205–13.

Huuskonen H, Lindbohm M L and Juutilainen J (1998a). Teratogenic and reproductive effects of low-frequency magnetic fields. *Mutat Res,* **410**(2), 167–83.

Huuskonen H, Juutilainen J, Julkunen A, Maki-Paakkanen J and Komulainen H (1998b). Effects of low-frequency magnetic fields on fetal development in CBA/Ca mice. *Bioelectromagnetics,* **19**(8), 477–85.

Huuskonen H, Juutilainen J and Komulainen H (2001a). Development of preimplantation mouse embryos after exposure to a 50 Hz magnetic field *in vitro*. *Toxicol Lett,* **122**(2), 149–55.

Huuskonen H, Saastamoinen V, Komulainen H, Laitinen J and Juutilainen J (2001b). Effects of low-frequency magnetic fields on implantation in rats. *Reprod Toxicol,* **15**(1), 49–59.

IARC (2002). Static and extremely low frequency electric and magnetic fields. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans,* Volume 80. Lyon, International Agency for Research on Cancer.

Ichioka S, Iwasaka M, Shibata M, Harii K, Kamiya A and Ueno S (1998). Biological effects of static magnetic fields on the microcirculatory blood flow *in vivo:* a preliminary report. *Med Biol Eng Comput,* **36**(1), 91–5.

Ichioka S, Minegishi M, Iwasaka M, Shibata M, Nakatsuka T, Harii K, Kamiya A and Ueno S (2000). High-intensity static magnetic fields modulate skin microcirculation and temperature *in vivo*. *Bioelectromagnetics,* **21**(3), 183–8.

ICNIRP (1994). Guidelines on limits of exposure to static magnetic fields. *Health Phys,* **66**(1), 100–106.

ICNIRP (1996). Health issues related to the use of hand-held radiotelephones and base transmitters. *Health Phys,* **70**, 587–93.

ICNIRP (1997). *Biological Effects of Static and ELF Electric and Magnetic Fields.* Proceedings International Seminar, Bologna, Italy, June 1997 (R Matthes, J H Bernhardt and M H Repacholi, eds). München, ICNIRP 4/97.

ICNIRP (1998). Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys,* **74**, 494–522.

ICNIRP (1999). *Health Effects of Electromagnetic Fields in the Frequency Range 300 Hz to 10 MHz.* Proceedings International Seminar, Maastricht, the Netherlands, June 1999 (R Matthes, E van Rongen and M Repacholi, eds). München, ICNIRP 8/99.

ICNIRP (2004). Exposure to Static and Low Frequency Electromagnetic Fields, Biological Effects and Health Consequences (0–100 kHz). München, ICNIRP.

ICNIRP/WHO (2003). Proceedings International Workshop: Weak Electric Field Effects in the Body (M H Repacholi and A F McKinlay, eds). *Radiat Prot Dosim,* **106**(4).

ICRP (2002). Basic anatomical and physiological data for use in radiological protection: reference values. ICRP Publication 89. *Ann ICRP,* **32**(Nos 3 and 4).

IEEE (1992). IEEE standard for safety levels with respect to human exposure to radio frequency electromagnetic fields, 3 kHz – 300 GHz. New York, IEEE, IEEE standard C95.1.

IEEE (2002). IEEE standard for safety levels with respect to human exposure to electromagnetic fields, 0–30 kHz. New York, IEEE, IEEE standard C95.6.

IEGMP (2000). Mobile Phones and Health. Report of an Independent Expert Group on Mobile Phones. Chilton, NRPB.

Iino M (1997). Effects of a homogeneous magnetic field on erythrocyte sedimentation and aggregation. *Bioelectromagnetics,* **18**(3), 215–22.

Ikehata M, Koana T, Suzuki Y, Shimizu H and Nakagawa M (1999). Mutagenicity and co-mutagenicity of static magnetic fields detected by bacterial mutation assay. *Mutat Res,* **427**(2), 147–56.

ILGRA (2002). United Kingdom Interdepartmental Liaison Group on Risk Assessment. The Precautionary Principle: Policy and Application. http://www.hse.gov.uk/dst/ilgra/pppa.htm.

Imaida K, Taki M, Yamaguchi T, Ito T, Watanabe S, Wake K, Aimoto A, Kamimura Y, Ito N and Shirai T (1998a). Lack of promoting effects of the electromagnetic near-field used for cellular phones (929.2 MHz) on rat liver carcinogenesis in a medium-term liver bioassay. *Carcinogenesis,* **19**, 311–14.

Imaida K, Taki M, Watanabe S, Kamimura Y, Ito T, Yamaguchi T, Ito N and Shirai T (1998b). The 1.5 GHz electromagnetic near-field used for cellular phones does not promote rat liver carcinogenesis in a medium-term liver bioassay. *Jpn J Cancer Res,* **89**, 995–1002.

Imaida K, Hagiwara A, Yoshino H, Tamano S, Sano M, Futakuchi M, Ogawa K, Asamoto M and Shirai T (2000). Inhibitory effects of low doses of melatonin on induction of preneoplastic liver lesions in a medium-term liver bioassay in F344 rats: relation to the influence of electromagnetic near field exposure. *Cancer Lett,* **55**, 105–14.

Imaida K, Kuzutani K, Wang J, Fujiwara O, Ogiso T, Kato K and Shirai T (2001). Lack of promotion of 7,12-dimethylbenz[a]anthracene-initiated mouse skin carcinogenesis by 1.5 GHz electromagnetic near fields. *Carcinogenesis,* **22**,1837–41.

Infante-Rivard C and Deadman J E (2003). Maternal occupational exposure to extremely low frequency magnetic fields during pregnancy and childhood leukemia. *Epidemiology,* **14**, 437–41.

INIRC (1994). International Non-Ionizing Radiation Committee of the International Radiation Protection Association, in collaboration with the International Labour Organization. Visual display units: radiation protection guidance. Geneva, International Labour Office.

Inskip P D (2001). Frequent radiation exposures and frequency-dependent effects: the eyes have it. *Epidemiology,* **12**, 1–4.

Inskip P D, Tarone R E, Hatch E E, Wilcosky T C, Shapiro W R, Selker R G, Fine H A, Black P M, Loeffler J S and Linet M S (2001). Cellular-telephone use and brain tumors. *N Engl J Med,* **344,** 79–86.

Inskip P D, Devesa S S and Fraumeni J F Jr (2003). Trends in the incidence of ocular melanoma in the United States, 1974–1998. *Cancer Causes Control,* **14**, 251–7.

Irgens A, Kruger K and Ulstein M (1999). The effect of male occupational exposure in infertile couples in Norway. *J Occup Environ Med,* **41**(12), 1116–20.

Ishido M, Nitta H, Kabuto M (2001). Magnetic fields (MF) of 50 Hz at 1.2 μT as well as 100 μT cause uncoupling of inhibitory pathways of adenylyl cyclase mediated by melatonin 1a receptor in MF-sensitive MCF-7 cells. *Carcinogenesis,* **22**(7), 1043–8.

ISO (1989). Hot environments – analytical determination and interpretation of thermal stress using calculation of required sweat rate. Geneva, International Standards Organization, ISO 7933.

Ivanov Ra, Naumova Pa, Radeva M, Vukova T and Radicheva N (2001). Effect of millimetre wave electromagnetic field on acetylcholinesterase activity of frog skeletal muscle. *Dokladi na B'lgarskata Akademiya na Naukite,* **54**, 91–4.

Ivanova V Yu, Martynova O V, Aleinik S V, and Limarenko A V (2000). Effect of modulated ultrahigh-frequency electromagnetic field and acoustic stimulation on the spectral characteristics of the cat brain electroncephalogram. *Biophysics,* **45**, 909–13.

Ivaschuk O I, Jones R A, Ishida-Jones T, Haggren W, Adey W R and Phillips J L (1997). Exposure of nerve growth factor-treated PC12 rat pheochromocytoma cells to a modulated radiofrequency field at 836.55 MHz: effects on c-jun and c-fos expression. *Bioelectromagnetics,* **18**, 223–9.

Iwasaka M, Ueno S and Tsuda H (1994). Effects of magnetic fields on fibrinolysis. *J Appl Phys,* **75**(10), 7162–4.

Iwasaka M, Takeuchi M, Ueno S and Tsuda H (1998). Polymerization and dissolution of fibrin under homogeneous magnetic fields. *IEEE Trans Magn,* **83**(11), 6453–5.

Iwasaka M, Takeuchi M and Ueno S (2000). Aggregation of blood platelets in static magnetic fields. *IEEE Trans Magn,* **36**(5), 3721–3.

Iwasaka M, Yaoita M, Kono T and Ueno S (2001). Magnetically disturbed activity of immobilized catalase on an electrode in hydrogen-peroxide buffer. *IEEE Trans Magn,* **37**(4), 2941–3.

Jacobson-Kram D, Tepper J, Kuo P, San R H, Curry P T, Wagner V O and Putman D L (1997). Evaluation of potential genotoxicity of pulsed electric and electromagnetic fields used for bone growth stimulation. *Mutat Res,* **388**(1), 45–57.

Jahreis G P, Johnson P G, Zhao Y L and Hui S W (1998). Absence of 60 Hz, 0.1-mT magnetic field-induced changes in oncogene transcription rates or levels in CEM-CM3 cells. *Biochim Biophys Acta,* **1443**(3), 334–42.

Jan L Y and Jan Y N (1989). Voltage-sensitive ion channels. *Cell,* **56**, 13–25.

Jankovic B D, Maric D, Ranin J and Veljic J (1991). Magnetic fields, brain and immunity: effect on humoral and cell-mediated immune responses. *Int J Neurosci,* **59**(1–3), 25–43.

Jankovic B D, Jovanova-Nesic K and Nikolic V (1993a). Locus ceruleus and immunity: III. Compromised immune function (antibody production, hypersensitivity skin reactions and experimental allergic encephalomyelitis) in rats with lesioned locus ceruleus is restored by magnetic fields applied to the brain. *Int J Neurosci,* **69**(1–4), 251–69.

Jankovic B D, Jovanova-Nesic K, Nikolic V and Nikolic P (1993b). Brain-applied magnetic fields and immune response: role of the pineal gland. *Int J Neurosci,* **70**(1–2), 127–34.

Jankovic B D, Nikolic P, Cupic V and Hladni K (1994). Potentiation of immune responsiveness in aging by static magnetic fields applied to the brain. Role of the pineal gland. *Ann NY Acad Sci,* **719**, 410–18.

Jauchem J R (1997). Exposure to extremely-low-frequency electromagnetic fields and radiofrequency radiation: cardiovascular effects in humans. *Int Arch Occup Environ Health,* **70**(1), 9–21.

Jauchem J R (1998). Health effects of microwave exposures: a review of the recent (1995–1998) literature. *J Microwave Power Electromagn Energy,* **33**(4), 263–74.

Jauchem J R, Ryan K L, Frei M R, Dusch S J, Lehnert H M and Kovatch R M (2001). Repeated exposure of C3H/HeJ mice to ultra-wideband electromagnetic pulses: lack of effects on mammary tumors. *Radiat Res,* **155**, 369–77.

Jech R, Sonka K, Ruzicka E, Nebuzelsky A, Bohm J, Juklickova M and Nevsimalova S (2001). Electromagnetic field of mobile phones affects visual event related potential in patients with narcolepsy. *Bioelectromagnetics,* **22**, 519–28.

Jefferys J G R (1994). Experimental neurobiology of epilepsies. *Curr Opin Neurol,* **7**, 113–22.

Jefferys J G R (1995). Nonsynaptic modulation of neuronal activity in the brain: electric currents and extracellular ions. *Physiol Rev,* **75**(4), 689–723.

Jefferys J G R, Deans J, Bikson M and Fox J (2003). Effects of weak electric fields on the activity of neurons and neuronal networks. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 321–4.

Jensh R P (1997). Behavioral teratologic studies using microwave radiation: is there an increased risk from exposure to cellular phones and microwave ovens? *Reprod Toxicol,* **11**, 601–11.

Jessen C (1987). Thermoregulatory mechanisms in severe heat stress and exercise. IN *Heat Stress: Physical Exertion and Environment* (J R S Hales and D A B Richards, eds). Elsevier Science Publishers BLV, pp 1–18.

Johansen C and Olsen J H (1998). Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers. *Am J Epidemiol,* **148**, 362–8.

Johansen, C, Boice, J, McLaughlin, J and Olsen, J (2001). Cellular telephones and cancer – a nationwide cohort study in Denmark. *J Natl Cancer Inst,* **93**, 203–7.

Johansen C, Boice J D, McLaughlin J K, Christensen H C and Olsen J H (2002a). Mobile phones and malignant melanoma of the eye. *Br J Cancer,* **86**, 348–9.

Johansen C, Feychting M, Moller M, Ornsbo P, Ahlbom A and Olsen J H (2002b). Risk of severe cardiac arrhythmia in male utility workers: a nationwide Danish cohort study. *Am J Epidemiol,* **156,** 857–61.

Johansson O, Hilliges M, Bjornhagen V and Hall K (1994). Skin changes in patients claiming to suffer from 'screen dermatitis': a two-case open-field provocation study. *Exp Dermatol,* **3**(5), 234–8.

Johansson O, Hilliges M and Han S W (1996). A screening of skin changes, with special emphasis on neurochemical marker antibody evaluation, in patients claiming to suffer from 'screen dermatitis' as compared to normal healthy controls. *Exp Dermatol,* **5**(5), 279–85.

Johansson O, Gangi S, Liang Y, Yoshimura K, Jing C and Liu P Y (2001). Cutaneous mast cells are altered in normal healthy volunteers sitting in front of ordinary TVs/PCs – results from open-field provocation experiments. *J Cutan Pathol,* **28**(10), 513–19.

John T M, Liu G Y and Brown G M (1998). 60 Hz magnetic field exposure and urinary 6-sulphatoxy-melatonin levels in the rat. *Bioelectromagnetics,* **19**(3), 172–80.

Jove M, Torrente M, Gilabert R, Espinar A, Cobos P and Piera V (1999). Effects of static electromagnetic fields on chick embryo pineal gland development. *Cells Tissues Organs,* **165**(2), 74–80.

Junkersdorf B, Bauer H and Gutzeit H O (2000). Electromagnetic fields enhance the stress response at elevated temperatures in the nematode *Caenorhabditis elegans. Bioelectromagnetics,* **21**(2), 100–106.

Juutilainen J (2003). Developmental effects of extremely low frequency electric and magnetic fields. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 385–90.

Juutilainen J and de Seze R (1998). Biological effects of amplitude-modulated radiofrequency radiation. *Scand J Work Environ Health,* **24**, 245–54.

Juutilainen J and Lang S (1997). Genotoxic, carcinogenic and teratogenic effects of electromagnetic fields. Introduction and overview. *Mutat Res,* **387**(3), 165–71.

Juutilainen J, Stevens R G, Anderson L E, et al (2000). Nocturnal 6-hydroxymelatonin sulfate excretion in female workers exposed to magnetic fields. *J Pineal Res,* **28**, 97–104.

Kalkstein L S and Greene J S (1997). An evaluation of climate/mortality relationships in large US cities and the possible impacts of a climate change. *Environ Health Perspect,* **105**, 84–93.

Kamimura Y, Saito K-i, Saiga T and Amenmiya Y (1994). Effect of 2.45 GHz microwave irradiation on monkey eyes. *IEICE Trans Commun,* **E77-B**, 762–5.

Kanal E, Gillen J, Evans JA, Savitz DA, Shellock FG (1993). Survey of reproductive health among female MR workers. *Radiology,* **187**(2), 395–9.

Kangarlu A, Burgess R E, Zhu H, Nakayama T, Hamlin R L, Abduljalil A M and Robataille P M L (1999). Cognitive, cardiac, and physiological safety studies in ultra high field magnetic resonance imaging. *Magn Reson Imaging,* **17**, 1407–16.

Karasek M and Lerchl A (2002). Melatonin and magnetic fields. *Neuroendocrinol Lett,* **23**(Suppl 1), 84–7.

Kato M and Shigemitsu T (1997). Effects of 50 Hz magnetic fields on pineal function in the rat. IN *The Melatonin Hypothesis, Breast Cancer and Use of Electric Power* (R G Stevens, B W Wilson and L E Anderson, eds). Richland, Battelle Press, pp 337–76.

Kato M, Honma K, Shigemitsu T and Shiga Y (1993). Effects of exposure to a circularly polarized 50 Hz magnetic field on plasma and pineal melatonin levels in rats. *Bioelectromagnetics,* **14**(2), 97–106.

Kato M, Honma K, Shigemitsu T and Shiga Y (1994a). Horizontal or vertical 50 Hz, 1 μT magnetic fields have no effect on pineal gland or plasma melatonin concentration of albino rats. *Neurosci Lett,* **168**(1–2), 205–8.

Kato M, Honma K, Shigemitsu T and Shiga Y (1994b). Circularly polarized 50 Hz magnetic field exposure reduces pineal gland and blood melatonin concentrations of Long-Evans rats. *Neurosci Lett,* **166**(1), 59–62.

Kato M, Honma K, Shigemitsu T and Shiga Y (1994c) Recovery of nocturnal melatonin concentration takes place within one week following cessation of 50 Hz circularly polarized magnetic field exposure for six weeks. *Bioelectromagnetics,* **15**(5), 489–92.

Kato M, Honma K, Shigemitsu T and Shiga Y (1994d). Circularly polarized, sinusoidal, 50 Hz magnetic field exposure does not influence plasma testosterone levels of rats. *Bioelectromagnetics,* **15**(6), 513–18.

Kavaliers M and Ossenkopp K P (1991). Opioid systems and magnetic field effects in the land snail, *Cepaea nemoralis. Biol Bull,* 180, 301–9.

Kavaliers M, Ossenkopp K P and Tysdale D M (1991). Evidence for the involvement of protein kinase C in the modulation of morphine-induced 'analgesia' and the inhibitory effects of exposure to 60 Hz magnetic fields in the snail, Cepaea nemoralis. *Brain Res,* **554**(1–2), 65–71.

Kavaliers M, Eckel L A and Ossenkopp K (1993). Brief exposure to 60 Hz magnetic fields improves sexually dimorphic spatial learning performance in the meadow vole, *Microtus Pennsylvanicus. J Comp Physiol [A],* **173**, 241–8.

Kavaliers M, Ossenkopp K P, Prato F S and Carson J J L (1994). Opioid systems and the biological effects of magnetic fields. IN *On the Nature of Electromagnetic Field Interactions with Biological Systems* (A H Frey, ed). Potomac MD, pp 181–94.

Kavaliers M, Ossenkopp K P, Prato F S, Innes D G, Galea L A, Kinsella D M and Perrot-Sinal T S (1996). Spatial learning in deer mice: sex differences and the effects of endogenous opioids and 60 Hz magnetic fields. *J Comp Physiol [A],* **179**(5), 715–24.

Kavaliers M, Wiebe J P and Ossenkopp K P (1998a). Brief exposure of mice to 60 Hz magnetic fields reduces the analgesic effects of the neuroactive steroid, 3alpha-hydroxy-4-pregnen-20-one. *Neurosci Lett,* **257**(3), 155–8.

Kavaliers M, Choleris E, Prato F S and Ossenkopp K (1998b). Evidence for the involvement of nitric oxide and nitric oxide synthase in the modulation of opioid-induced antinociception and the inhibitory effects of exposure to 60 Hz magnetic fields in the land snail. *Brain Res,* **809**(1), 50–57.

Kazantzis N, Podd J and Whittington C (1996). Acute effects of 50 Hz, 100 μT magnetic field exposure on visual duration discrimination at two different times of the day. *Bioelectromagnetics,* **19**, 310–17.

Keatinge W R, Coleshaw S R K, Easton J C, Cotter F, Mattock M B and Chelliah R (1986). Increased platelet and red cell counts, blood viscosity and plasma cholesterol level during heat stress, and mortality from coronary and cerebral thromboses. *Am J Med,* **81**, 795–800.

Keatinge W R, Donaldson G C, Cordioli E, Martinelli M, Kunst A E, Mackenbach J P, Nayha S and Vuori I (2000). Heat related mortality in warm and cold regions of Europe: observational study. *Br Med J,* **321**, 670–73.

Keetley V, Wood A, Sadafi H and Stough C (2001). Neuropsychological sequelae of 50 Hz magnetic fields. *Int J Radiat Biol,* **77**(6), 735–42.

Kelman B J, Abernethy C S, Carlile D W, Decker J R Jr, Kalkwarf D R, Kuffel E G, Mahlum D D, Skalski J R and Strand J A (1983). Biological effect of magnetic fields. IN Pacific Northwest Laboratory Annual Report for 1982 to the DOE Office of Energy Research. Part 1 Biomedical Sciences. PNL-4600 PT1. Richland, Pacific Northwest Laboratory, 113.

Kenny W L (1985). Physiological correlates of heat intolerance. *Sports Med,* **2**, 279–86.

Khadir R, Morgan J L and Murray J J (1999). Effects of 60 Hz magnetic field exposure on polymorphonuclear leukocyte activation. *Biochim Biophys Acta,* **1472**(1–2), 359–67.

Khalil A M, Qassem W F and Suleiman M M (1993). A preliminary study on the radiofrequency field-induced cytogenetic effects in cultured human lymphocytes. *Dirasat,* **20**, 121–130.

Kharazi A I, Babbitt J T and Hahn T J (1999). Primary brain tumor incidence in mice exposed to split-dose ionizing radiation and circularly polarized 60 Hz magnetic fields. *Cancer Lett,* **147**(1–2), 149–56.

Kheifets L (1999). Occupational exposure assessment in epidemiological studies of EMF. *Radiat Prot Dosim,* **83**, 61–9.

Khillare B and Behari J (1998). Effect of amplitude-modulated radiofrequency radiation on reproduction pattern in rats. *Electro- Magnetobiol,* **17**(1), 43.

Kinouchi Y, Yamaguchi H and Tenforde T S (1996). Theoretical analysis of magnetic field interactions with aortic blood flow. *Bioelectromagnetics,* **17**, 21–32.

Klimesch W, Pfurtscheller G and Schimke H (1992). Pre- and poststimulus processes in category judgement task as measured by event-related desynchronization. *J Psychophysiol,* **6**, 185–203.

Kliukiene J, Tynes T and Andersen A (2003). Follow-up of radio and telegraph operators with exposure to electromagnetic fields and risk of breast cancer. *Eur J Cancer Prev,* **12**, 301–7.

Koivisto M, Revonsuo A, Krause C, Haarala C, Sillanmaki L, Laine M and Hamalainen H (2000a). Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. *Neuroreport,* **11** (2), 413–15.

Koivisto M, Krause C M, Revonsuo A, Laine M and Hamalainen H (2000b). The effects of electromagnetic field emitted by GSM phones on working memory. *Neuroreport,* **11** (8), 1641–3.

Koivisto M, Haarala C, Krause C M, Revonsuo A, Laine M and Hamalainen H (2001). GSM phone signal does not produce subjective symptoms. *Bioelectromagnetics,* **22** (3), 212–15.

Konermann G and Monig H (1986). Studies on the influence of static magnetic fields on prenatal development of mice. *Radiologe,* **26**, 490 (in German).

Korpinen L and Partanen J (1994a). The influence of 50 Hz electric and magnetic fields on the extrasystoles of human heart. *Rev Environ Health,* **10** (2), 105–12.

Korpinen L and Partanen J (1994b). Influence of 50 Hz electric and magnetic fields on the pulse rate of human heart. *Bioelectromagnetics,* **15** (6), 503–12.

Korpinen L and Partanen J (1996). Influence of 50 Hz electric and magnetic fields on human blood pressure. *Radiat Environ Biophys,* **35** (3), 199–204.

Korpinen L, Partanen J and Uusitalo A (1993). Influence of 50 Hz electric and magnetic fields on the human heart. *Bioelectromagnetics,* **14** (4), 329–40.

Kotani H, Iwasaka M, Curtis A and Ueno S (2000). Magnetic orientation of collagen and bone mixture. *J Appl Phys,* **87** (9), 6191–3.

Kotte A, van Leeuwen G, de Bree J, van der Koijk J, Crezee H and Lagendijk J (1996). A description of discrete vessel segments in thermal modelling of tissues. *Phys Med Biol,* **41**, 865–84.

Kowalczuk C I, Sienkiewicz Z J and Saunders R D (1991). Biological effects of exposure to non-ionising electromagnetic fields and radiation: I. static electric and magnetic fields. Chilton, NRPB-R238.

Kowalczuk C I, Robbins L, Thomas J M, Butland B K and Saunders R D (1994). Effects of prenatal exposure to 50 Hz magnetic fields on development in mice: I. Implantation rate and fetal development. *Bioelectromagnetics,* **15** (4), 349–61.

Krause C M, Sillanmaki L, Koivisto M, Haggqvist A, Saarela C, Revonsuo A, Laine M and Hamalainen H (2000a). Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task. *Neuroreport,* **11** (4), 761–4.

Krause C M, Sillanmaki L, Koivisto M, Haggqvist A, Saarela C, Revonsuo A, Laine M and Hamalainen H (2000b). Effects of electromagnetic fields emitted by cellular phones on the electroencephalogram during a visual working memory task. *Int J Radiat Biol,* **76** (12), 1659–67.

Krewski D, Byus C V, Glickman B W, Lotz W G, Mandeville R, McBride M L, Prato F S and Weaver D F (2001a). Potential health risks of radiofrequency fields from wireless telecommunication devices. *J Toxicol Environ Health B Crit Rev,* **4**, 1–143.

Krewski D, Byus C V, Glickman B W, Lotz W G, Mandeville R, McBride M L, Prato F S and Weaver D F (2001b). Recent advances in research on radiofrequency fields and health. *J Toxicol Environ Health B Crit Rev,* **4**, 145–59.

Kroeker G, Parkinson D, Vriend J and Peeling J (1996). Neurochemical effects of static magnetic field exposure. *Surg Neurol,* **45** (1), 62–6.

Kues H A and Monahan J C (1992). Microwave-induced changes in the primate eye. *Johns Hopkins APL Technical Digest,* **13**, 244–54.

Kues H A, Hirst L W, Lutty G A, D'Anna S A and Dunkelberger G R (1985). Effects of 2.45 GHz microwaves on primate corneal endothelium. *Bioelectromagnetics,* **6**, 177–88.

Kues H A, Monohan J C, D'Anna S A, McLeod D S, Lutty G A and Koslov S (1992). Increased sensitivity of the non-human primate eye to microwave radiation following ophthalmic drug pretreatment. *Bioelectromagnetics,* **13**, 379–93.

Kues H A, D'Anna S A, Osiander R, Gren W R and Monohan J C (1999). Absence of ocular effects after either single or repeated exposure to 10 mW/cm^2 form a 60 GHz CW source. *Bioelectromagnetics,* **20**, 463–73.

Kumlin T, Kosma V M, Alhonen L, Janne J, Komulainen H, Lang S, Rytomaa T, Servomaa K and Juutilainen J (1998a). Effects of 50 Hz magnetic fields on UV-induced skin tumourigenesis in ODC-transgenic and non-transgenic mice. *Int J Radiat Biol,* **73**(1), 113–21.

Kumlin T, Alhonen L, Janne J, Lang S, Kosma V M and Juutilainen J (1998b). Epidermal ornithine decarboxylase and polyamines in mice exposed to 50 Hz magnetic fields and UV radiation. *Bioelectromagnetics,* **19**, 388–91.

Kumlin T, Heikkinen P, Kosma VM, Alhonen L, Jänne J and Juutilainen J (2002). p53-independent apoptosis in UV-irradiated mouse skin: possible inhibition by 50 Hz magnetic fields. *Radiat Environ Biophys,* **41**, 155–8.

Kurokawa Y, Nitta H, Imai H and Kabuto M (2003). Acute exposure to 50 Hz magnetic fields with harmonics and transient components: lack of effects on nighttime hormonal secretion in men. *Bioelectromagnetics,* **24**, 12–20.

Kwee S and Raskmark P (1998). Changes in cell proliferation due to environmental non-ionizing radiation: 2. Microwave radiation. *Bioelectrochem Bioenerg,* **44**, 251–5.

Kwee S, Raskmark P and Velizarov S (2001). Changes in cellular proteins due to environmental non-ionizing radiation: 1. Heat shock proteins. *Electro- Magnetobiol,* **20**, 165–76.

La Regina M, Moros E G, Pickard W F, Straube W L, Baty J and Roti Roti J L (2003). The effect of chronic exposure to 835.62 MHz FDMA or 847.74 MHz CDMA radiofrequency radiation on the incidence of spontaneous tumors in rats. *Radiat Res,* **160**, 143–51.

Laburn H P, Mitchell D and Goelst K (1992). Fetal and maternal body temperatures measured by radiotelemetry in near-term sheep during thermal stress. *J Appl Physiol,* **72**, 894–900.

Lacy-Hulbert A, Metcalfe J C and Hesketh R (1998). Biological responses to electromagnetic fields. *FASEB J,* **12**(6), 395–420.

Lacy-Hulbert A, Wilkins R C, Hesketh T R and Metcalfe J C (1995). No effect of 60 Hz electromagnetic fields on MYC or beta-actin expression in human leukemic cells. *Radiat Res,* **144**(1), 9–17.

Lai H (1992). Research on the neurological effects of nonionizing radiation at the University of Washington. *Bioelectromagnetics,* **13**, 513–26.

Lai H (1996). Spatial learning deficit in the rat after exposure to a 60 Hz magnetic field. *Bioelectromagnetics,* **17**(6), 494–6.

Lai H (2001). Memory and Behaviour. IN *Biological Effects, Health Consequences and Standards for Pulsed Radiofrequency Fields* (R Matthes, J H Bernhardt and M H Repacholi, eds). München, ICNIRP 11/2001, pp 193–209.

Lai H and Carino M (1998). Intracerebroventricular injection of mu- and delta-opiate receptor antagonists block 60 Hz magnetic field-induced decreases in cholinergic activity in the frontal cortex and hippocampus of the rat. *Bioelectromagnetics,* **19**(7), 432–7.

Lai H and Carino M (1999). 60 Hz magnetic fields and central cholinergic activity: effects of exposure intensity and duration. *Bioelectromagnetics,* **20**(5), 284–9.

Lai H and Singh N P (1995). Acute, low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells. *Bioelectromagnetics,* **16**, 207–10.

Lai H and Singh N P (1996). Single- and double-strand breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation. *Int J Radiat Biol,* **69**, 513–21.

Lai H and Singh NP (1997a). Acute exposure to a 60 Hz magnetic field increases DNA strand breaks in rat brain cells. *Bioelectromagnetics,* **18**(2), 156–65.

Lai H and Singh N P (1997b). Melatonin and N-tert-butyl-alpha-phenylnitrone block 60 Hz magnetic field-induced DNA single and double strand breaks in rat brain cells. *J Pineal Res,* **22**, 152–62.

Lai H and Singh N P (1997c). Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells. *Bioelectromagnetics,* **18**, 446–54.

Lai H, Carino M A, Horita A and Guy A W (1989). Low-level microwave irradiation and central cholinergic systems. *Pharmacol Biochem Behav,* **33**, 131–8.

Lai H, Carino M A, Horita A and Guy A W (1992a). Single vs. repeated microwave exposure: Effects on benzodiazepine receptors in the brain of the rat. *Bioelectromagnetics,* **13**, 57–66.

Lai H, Carino M A, Horita A and Guy A W (1992b). Opioid receptor subtypes that mediate a microwave-induced decrease in central cholinergic activity in the rat. *Bioelectromagnetics,* **13**, 237–46.

Lai H, Carino M A, Horita A and Guy A W (1993). Effects of a 60 Hz magnetic field on central cholinergic systems of the rat. *Bioelectromagnetics,* **14**(1), 5–15.

Lai H, Horita A and Guy A W (1994). Microwave irradiation affects radial-arm maze performance in the rat. *Bioelectromagnetics,* **15**, 95–104.

Lai H, Carino M A, Horita A and Guy A W (1996). Intraseptal microinjection of beta-funaltrexamine blocked a microwave-induced decrease of hippocampal cholinergic activity in the rat. *Pharmacol Biochem Behav,* **53**, 613–16.

Lai H, Carino M A and Ushijima I (1998). Acute exposure to a 60 Hz magnetic field affects rats' water-maze performance. *Bioelectromagnetics,* **19**(2), 117–22.

Lagroye I and Poncy J L (1997). The effect of 50 Hz electromagnetic fields on the formation of micronuclei in rodent cell lines exposed to gamma radiation. *Int J Radiat Biol,* **72**(2), 249–54.

Lagroye I and Poncy J L (1998). Influences of 50 Hz magnetic fields and ionizing radiation on c-jun and c-fos oncoproteins. *Bioelectromagnetics,* **19**(2), 112–16.

Lakatta E G (2002). Age-associated cardiovascular changes in health: impact on cardiovascular disease in older persons. Heart Failure Rev, **7**(1), 29–49.

Landry P S, Sadasivan K K, Marino A A and Albright J A (1997). Electromagnetic fields can affect osteogenesis by increasing the rate of differentiation. *Clin Orthop,* **338**, 262–70.

Lass J, Tuulik V, Ferenets R, Riisalo R and Hinrikus H (2002). Effects of 7 Hz-modulated 450 MHz electromagnetic radiation on human performance in visual memory tasks. *Int J Radiat Biol,* **78**(10), 937–44.

Lebedeva N N, Sulimov A V, Sulimova O P, Korotkovskaya T I and Gailus T (2001). Investigation of brain potentials in sleeping humans exposed to the electromagnetic field of mobile phones. *Crit Rev Biomed Eng,* **29**(1), 125–33.

Lee G M, Neutra R R, Hristova L, Yost M and Hiatt R A (2000). The use of electric bed heaters and the risk of clinically recognized spontaneous abortion. *Epidemiology,* **11**, 406–15.

Lee G M, Neutra R R, Hristova L, Yost M and Hiatt R A (2002). A nested case–control study of residential and personal magnetic field measures and miscarriages. *Epidemiology,* **13**, 21–31.

Lee J M Jr, Stormshak F, Thompson J M, Thinesen P, Painter L J, Olenchek E G, Hess D L, Forbes R and Foster D L (1993). Melatonin secretion and puberty in female lambs exposed to environmental electric and magnetic fields. *Biol Reprod,* **49**(4), 857–64.

Lee J M Jr, Stormshak F, Thompson J M, Hess D L and Foster D L (1995). Melatonin and puberty in female lambs exposed to EMF: a replicate study. *Bioelectromagnetics,* **16**(2), 119–23.

Lee T M, Ho S M, Tsang L Y, Yang S H, Li L S, Chan C C and Yang S Y (2001). Effect on human attention of exposure to the electromagnetic field emitted by mobile phones. *Neuroreport,* **12**(4), 729–31.

Leitgeb N and Schröttner J (2003). Electrosensibility and electromagnetic hypersensitivity. *Bioelectromagnetics,* **24**, 387–94.

Leszczynski D, Joenvaara S, Reivinen J and Kuokka R (2002). Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: molecular mechanism for cancer- and blood–brain barrier-related effects. *Differentiation,* **70**(2–3), 120–29.

Levallois P (2002). Hypersensitivity of human subjects to environmental electric and magnetic field exposure: A review of the literature. *Environ Health Perspect,* **110**(Suppl 4), 613–18.

Levin M and Ernst S G (1997). Applied DC magnetic fields cause alterations in the time of cell divisions and developmental abnormalities in early sea urchin embryos. *Bioelectromagnetics,* **18**(3), 255–63.

Levine R L and Bluni T D (1994). Magnetic field effects on spatial discrimination learning in mice. *Physiol Behav,* **55**(3), 465–7.

Li C-Y and Sung F-C (2003). Association between occupational exposure to power frequency electromagnetic fields and amyotrophic lateral sclerosis: a review. *Am J Ind Med,* **43**, 212–20.

Li CY, Lin RS and Sung FC (2003). Elevated residential exposure to power frequency magnetic field associated with greater average age at diagnosis for patients with brain tumors. *Bioelectromagnetics,* **24**, 218–21.

Li D-K and Neutra,R R (2002). Magnetic fields and miscarriage. *Epidemiology*, **13**, 237–8.

Li D-K, Odouli R, Wi S, Janevic T, Golditch I, Bracken T D, Senior R, Rankin R and Iriye R (2002). A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of miscarriage. *Epidemiology,* **13,** 9–20.

Li L, Bisht K S, LaGroye I, Zhang P, Straube W L, Moros E G and Roti Roti J L (2001). Measurement of DNA damage in mammalian cells exposed *in vitro* to radiofrequency fields at SARs of 3–5 W/kg. *Radiat Res,* **156**, 328–32.

Liboff A R, Thomas J R and Schrot J (1989). Intensity threshold for 60 Hz magnetically induced behavioral changes in rats. *Bioelectromagnetics,* **10**(1), 111–13.

Liburdy R P and Levine G A (1998). Magnetic fields and formation of organized structures in normal human mammary cells. IN BEMS Annual Meeting.

Liburdy R P, Sloma T R, Sokolic R and Yaswen P (1993). ELF magnetic fields, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER+ breast cancer cell proliferation. *J Pineal Res,* **14**(2), 89–97.

Liddle C G, Putnam J P and Huey O P (1994). Alteration of life span of mice chronically exposed to 2.45 GHz CW microwaves. *Bioelectromagnetics*, **15**, 177–81.

Linder-Aronson A and Lindskog S (1995). Effects of static magnetic fields on human periodontal fibroblasts *in vitro*. *Swed Dent J,* **19**(4), 131–7.

Lindstrom E, Lindstrom P, Berglund A, Mild K H and Lundgren E (1993). Intracellular calcium oscillations induced in a T-cell line by a weak 50 Hz magnetic field. *J Cell Physiol,* **156**(2), 395–8.

Lindstrom E, Berglund A, Mild K H, Lindstrom P and Lundgren E (1995a). CD45 phosphatase in Jurkat cells is necessary for response to applied ELF magnetic fields. *FEBS Lett,* **370**(1–2), 118–22.

Lindstrom E, Lindstrom P, Berglund A, Lundgren E and Mild K H (1995b). Intracellular calcium oscillations in a T-cell line after exposure to extremely-low-frequency magnetic fields with variable frequencies and flux densities. *Bioelectromagnetics,* **16**(1), 41–7.

Litovitz T A, Krause D and Mullins J M (1991). Effect of coherence time of the applied magnetic field on ornithine decarboxylase activity. *Biochem Biophys Res Commun,* **178**(3), 862–5.

Litovitz T A, Krause D, Penafiel M, Elson E C and Mullins J M (1993). The role of coherence time in the effect of microwaves on ornithine decarboxylase activity. *Bioelectromagnetics,* **14**, 395–403.

Lloyd D, Hone P, Edwards A, Cox R and Halls J (in press). The repair of γ-ray induced chromosomal damage in human lymphocytes after exposure to extremely low frequency electromagnetic fields. *Cytogenet Genome Res*.

Loberg L I, Gauger J R, Buthod J L, Engdahl W R and McCormick D L (1999). Gene expression in human breast epithelial cells exposed to 60 Hz magnetic fields. *Carcinogenesis,* **20**(8), 1633–6.

Lonne-Rahm S, Andersson B, Melin L, Schultzberg M, Arnetz B and Berg M (2000). Provocation with stress and electricity of patients with 'sensitivity to electricity'. *J Occup Environ Med,* **42**(5), 512–16.

Lorrain J-L and Raoul D (2002). Téléphonie mobile et santé. Office Parliamentaire D'Évaluation des Choix Scientifiques et Technologiques. Assemblée Nationale No. 346, Sénat No. 52.

Löscher W (2001). Do cocarcinogenic effects of ELF electromagnetic fields require repeated long-term interaction with carcinogens? Characteristics of positive studies using the DMBA breast cancer model in rats. *Bioelectromagnetics,* **22**(8), 603–14.

Löscher W and Käs G (1998). Extraordinary behaviour disorders in cows in proximity to transmission stations. *Der Praktische Tierarzt,* **79**(5), 437–44.

Löscher W and Mevissen M (1994). Animal studies on the role of 50/60-hertz magnetic fields in carcinogenesis. *Life Sci,* **54**(21), 1531–43.

Löscher W and Mevissen M (1995). Linear relationship between flux density and tumor co-promoting effect of prolonged magnetic field exposure in a breast cancer model. *Cancer Lett,* **96**(2), 175–80.

Löscher W, Mevissen M, Lehmacher W and Stamm A (1993). Tumor promotion in a breast cancer model by exposure to a weak alternating magnetic field. *Cancer Lett,* **71**(1–3), 75–81.

Löscher W, Wahnschaffe U, Mevissen M, Lerchl A and Stamm A (1994). Effects of weak alternating magnetic fields on nocturnal melatonin production and mammary carcinogenesis in rats. *Oncology,* **51**(3), 288–95.

Löscher W, Mevissen M and Lerchl A (1998). Exposure of female rats to a 100 μT 50 Hz magnetic field does not induce consistent changes in nocturnal levels of melatonin. *Radiat Res,* **150**(5), 557–67.

Lovely R H (1988). Recent studies in the behavioral toxicology of ELF electric and magnetic fields. *Prog Clin Biol Res,* **257**, 327–47.

Lovely R H, Creim J A, Kaune W T, Miller M C, Phillips R D and Anderson L E (1992). Rats are not aversive when exposed to 60 Hz magnetic fields at 3.03 mT. *Bioelectromagnetics,* **13**(5), 351–62.

Lövsund P, Öberg P A and Nilsson S E G (1980). Magneto- and electrophosphenes: a comparative study. *Med Biol Eng Comput* **18**, 758–64.

Lu S-T, Mathur S P, Stuck B, Zwick H, D'Andrea J A, Ziriax J M, Merritt J H, Lutty G, McLeod D S and Johnson M (2000). Effects of high peak power microwaves on the retina of the rhesus monkey. *Bioelectromagnetics,* **21**, 439–54.

Lundsberg L S, Bracken M B and Belanger K (1995). Occupationally related magnetic field exposure and male subfertility. *Fertil Steril,* **63**, 384–91.

Lydahl E and Phillipson B (1984). Infrared radiation and cataract: II. Epidemiologic investigation of glassworkers. *Acta Ophthalmol,* **62**, 976–92.

Lyle D B, Fuchs T A, Casamento J P, Davis C C and Swicord M L (1997). Intracellular calcium signaling by Jurkat T-lymphocytes exposed to a 60 Hz magnetic field. *Bioelectromagnetics,* **18**(6), 439–45.

Lyskov E, Juutilainen J, Jousmaki V, Hanninen O, Medvedev S and Partanen J (1993a). Influence of short-term exposure of magnetic field on the bioelectrical processes of the brain and performance. *Int J Psychophysiol,* **14**(3), 227–31.

Lyskov E B, Juutilainen J, Jousmaki V, Partanen J, Medvedev S and Hanninen O (1993b). Effects of 45 Hz magnetic fields on the functional state of the human brain. *Bioelectromagnetics,* **14**(2), 87–95.

Lyskov E, Sandström M and Hansson Mild K (2001a). Neurophysiological study of patients with perceived 'electrical hypersensitivity'. *Int J Psychophysiol,* **42**(3), 233–41.

Lyskov E, Sandström M and Mild K H (2001b). Provocation study of persons with perceived electrical hypersensitivity and controls using magnetic field exposure and recording of electrophysiological characteristics. *Bioelectromagnetics,* **22**(7), 457–62.

McCann J, Dietrich F, Rafferty C, Martin AO (1993). A critical review of the genotoxic potential of electric and magnetic fields. *Mutat Res,* **297**(1), 61-95.

McCann J, Dietrich F and Rafferty C (1998). The genotoxic potential of electric and magnetic fields: an update. *Mutat Res,* **411**(1), 45–86.

McCann J, Kavet R and Rafferty C N (2000). Assessing the potential carcinogenic activity of magnetic fields using animal models. *Environ Health Perspect,* **108**(Suppl 1), 79–100.

McCormick D L, Cahill M A, Ryan B M, Findlay J C and Boorman G A (1995). Pineal function in B6C3F1 mice exposed to 60 Hz magnetic fields: time course studies. IN Abstracts, 17th Annual Meeting of the Bioelectromagnetics Society, June 1995, Boston, Massachusetts, p 81.

McCormick D L, Ryan B M, Findley J C, Gauger J R, Johnson T R, Morrissey R L and Boorman G A (1998). Exposure to 60 Hz magnetic fields and risk of lymphoma in PIM transgenic and TSG-p53 (p53 knockout) mice. *Carcinogenesis,* **19**(9), 1649–53.

McCormick D L, Boorman G A, Findlay J C, Hailey J R, Johnson T R, Gauger J R, Pletcher J M, Sills R C and Haseman J K (1999). Chronic toxicity/oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in B6C3F1 mice. *Toxicol Pathol,* **27**(3), 279–85.

McKay B E, Persinger M A (2000). Application timing of complex magnetic fields delineates windows of posttraining-pretesting vulnerability for spatial and motivational behaviors in rats. *Int J Neurosci,* **103**(1–4), 69–77.

McKinlay A F, Bach Andersen J, Bernhardt J H, Grandolfo M, Hossman K-A, van Leeuwen F E, Hansson Mild K, Swerdlow A J, Verschaeve L and Veyret B (1996). Possible Health Effects Related to the Use of Radiotelephones. European Commission Expert Group Report. Brussels, European Commission, http://europa.eu.int/ISPO/infosoc/telecompolicy/en/Studyhr.doc.

McLauchlan K A (1981). The effects of magnetic fields on chemical reactions. *Sci Prog (Oxford),* **67**, 509.

McLean J R, Stuchly M A, Mitchel R E, Wilkinson D, Yang H, Goddard M, Lecuyer D W, Schunk M, Callary E and Morrison D (1991). Cancer promotion in a mouse-skin model by a 60 Hz magnetic field: II. Tumor development and immune response. *Bioelectromagnetics,* **12**(5), 273–87.

McLean J, Thansandote A, Lecuyer D, Goddard M, Tryphonas L, Scaiano J C and Johnson F (1995). A 60 Hz magnetic field increases the incidence of squamous cell carcinomas in mice previously exposed to chemical carcinogens. *Cancer Lett,* **92**(2), 121–5.

McLean J R, Thansandote A, Lecuyer D and Goddard M (1997). The effect of 60 Hz magnetic fields on co-promotion of chemically induced skin tumors on SENCAR mice: a discussion of three studies. *Environ Health Perspect,* **105**(1), 94–6.

McLeod K J and Collazo L (2000). Suppression of a differentiation response in MC-3T3-E1 osteoblast-like cells by sustained, low-level, 30 Hz magnetic-field exposure. *Radiat Res,* **153**(5 Part 2), 706–14.

McNamee J P, Bellier P V, McLean J R N, Gajda G B and Thansandote A (2000). DNA damage and apoptosis in the immature mouse cerebellum after acute exposure to a 1 mT, 60 Hz magnetic field. *Mutat Res,* **513**, 121–33.

McNamee J P, Bellier P V, Gajda G B, Lavallee B F, Lemay E P, Marro L and Thansandote A (2002a). DNA damage in human leukocytes after acute *in vitro* exposure to a 1.9 GHz pulse-modulated radiofrequency field. *Radiat Res,* **158**, 534–7.

McNamee J P, Bellier P V, Gajda G B, Miller S M, Lemay E P, Lavallee B F, Marro L and Thansandote A (2002b). DNA damage and micronucleus induction in human leukocytes after acute *in vitro* exposure to a 1.9 GHz continuous-wave radiofrequency field. *Radiat Res,* **158**, 523–33.

Maes A, Verschaeve L, Arroyo A, De Wagter C and Vercruyssen L (1993). *In vitro* cytogenetic effects of 2450 MHz waves on human peripheral blood lymphocytes. *Bioelectromagnetics,***14**, 495–501.

Maes A, Collier M, Slaets D and Verschaeve L (1995). Cytogenetic effects of microwaves from mobile communication frequencies (954 MHz). *Electro- Magnetobiol,* **14**, 91–8.

Maes A, Collier M, Van Gorp U, Vandoninck S and Verschaeve L (1997). Cytogenetic effects of 935.2 MHz (GSM) microwaves alone and in combination with mitomycin C. *Mutat Res,* **393**, 151–6.

Maes A, Collier M and Verschaeve L (2001). Cytogenetic effects of 900 MHz (GSM) microwaves on human lymphocytes. *Bioelectromagnetics,* **22**, 91–6.

Magin R L, Lee J K, Klintsova A, Carnes K I and Dunn F (2000). Biological effects of long-duration, high-field (4 T) MRI on growth and development in the mouse. *J Magn Reson Imaging,* **12**(1), 140–49.

Magras I N and Xenos T D (1997). RF radiation-induced changes in the prenatal development of mice. *Bioelectromagnetics,* **18**, 455–61.

Mahdi A, Gowland P A, Mansfield P, Coupland R E and Lloyd R G (1994). The effects of static 3.0 T and 0.5 T magnetic fields and the echo-planar imaging experiment at 0.5 T on *E coli. Br J Radiol,* **67**(802), 983–7.

Mahlum D D, Sikov M R and Decker J R (1979). Dominant lethal studies in mice exposed to direct-current magnetic fields. IN *Biological Effects of Extremely Low Frequency Electromagnetic Fields* (R D Phillips, M F Gillis, W T Kaune and D D Mahlum, eds). 18th Hanford Life Sciences Symposium, Richland, Washington, October, 1978. Springfield VA, Department of Energy, National Technical Information Service, p 474.

Malchaire J, Kampman B, Havenith G, Mehnert P and Genhardt H J (2000). Criteria for estimating acceptable exposure times in hot working environments: a review. *Int Arch Occup Environ Health,* **73**, 215–20.

Malchaire J, Kampmann B, Mehnert P Gebhardt H, Piette A, Havenith G, Holmér I, Parsons K, Alfono G and Griefahn B (2002). Assessment of the risk of heat disorders encountered during work in hot conditions. *Int Arch Occup Environ Health,* **75**, 153–62.

Malyapa R S, Ahern E W, Straube W L, Moros E G, Pickard W F and Roti Roti J L (1997a). Measurement of DNA damage after exposure to 2450 MHz electromagnetic radiation. *Radiat Res,* **148**, 608–61.

Malyapa R S, Ahern E W, Straube W L, Moros E G, Pickard W F and Roti Roti J L (1997b). Measurement of DNA damage after exposure to electromagnetic radiation in the cellular phone communication frequency band (835.62 and 847.74 MHz). *Radiat Res,* **148**, 618–27.

Malyapa R S, Ahern E W, Bi C, Straube W L, LaRegina M, Pickard W F and Roti Roti J L (1998). DNA damage in rat brain cells after *in vivo* exposure to 2450 MHz electromagnetic radiation and various methods of euthanasia. *Radiat Res,* **149**, 637–45.

Mandeville R, Franco E, Sidrac-Ghali S, Paris-Nadon L, Rocheleau N, Mercier G, Desy M and Gaboury L (1997). Evaluation of the potential carcinogenicity of 60 Hz linear sinusoidal continuous-wave magnetic fields in Fischer F344 rats. *FASEB J,* **11**(13), 1127–36.

Mandeville R, Franco E, Sidrac-Ghali S, Paris-Nadon L, Rocheleau N, Mercier G, Desy M, Devaux C and Gaboury L (2000). Evaluation of the potential promoting effect of 60 Hz magnetic fields on N-ethyl-N-nitrosourea induced neurogenic tumors in female F344 rats. *Bioelectromagnetics,* **21**(2), 84–93.

Mann K and Roschke J (1996). Effects of pulsed high-frequency electromagnetic fields on human sleep. *Neuropsychobiology,* **33**(1), 41–7.

Mann K, Roschke J, Connemann B and Beta H (1998a). No effects of pulsed high-frequency electromagnetic fields on heart rate variability during human sleep. *Neuropsychobiology,* **38**(4), 251–6.

Mann K, Wagner P, Brunn G, Hassan F, Hiemke C and Roschke J (1998b). Effects of pulsed high-frequency electromagnetic fields on the neuroendocrine system. *Neuroendocrinology,* **67**(2), 139–44.

Maresh C M, Cook M R, Cohen H D, Graham C and Gunn W S (1988). Exercise testing in the evaluation of human responses to powerline frequency fields. *Aviat, Space Environ Med,* **59**(12), 1139–45.

Margonato V, Nicolini P, Conti R, Zecca L, Veicsteinas A and Cerretelli P (1995). Biologic effects of prolonged exposure to ELF electromagnetic fields in rats: II. 50 Hz magnetic fields. *Bioelectromagnetics,* **16**(6), 343–55.

Marino A A, Bell G B and Chesson A (1996). Low-level EMFs are transduced like other stimuli. *J Neurol Sci,* **144**(1–2), 99–106.

Martens W J M (1998). Climate change, thermal stress and mortality changes. *Soc Sci Med,* **46**, 331–44.

Mason P A, Ziriax J M, Hurt W D and D'Andrea J W (1999). 3-dimensional models for EMF dosimetry. IN *Electricity and Magnetism in Biology and Medicine* (F Bersani, ed). New York,Kluwer Academic/Plenum, pp 291–4.

Mason P A, Hurt W D, Walters T J, D'Andrea J W, Gajsek P, Ryan K L, Nelson D A, Smith K I and Ziriax J M (2000). Effects of frequency, permittivity and voxel size on predicted specific absorption rate values in biological tissue during electromagnetic-field exposure. *IEEE Trans Microwave Theory Techniq,* **48**(11), 2050–58.

Mason P A, Walters T J, DiGiovanni J, Beason C W, Jauchem J R, Dick E J Jr, Mahajan K, Dusch S J, Shields B A, Merritt J H, Murphy M R and Ryan K L (2001). Lack of effect of 94 GHz radio frequency radiation exposure in an animal model of skin carcinogenesis. *Carcinogenesis,* **22**, 1701–8.

Mathie A, Kennard L E and Veale E L (2003). Neuronal ion channels and their sensitivity to extremely low frequency weak electric field effects. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 311–16.

Mausset A L, de Seze R, Montpeyroux F and Privat A (2001). Effects of radiofrequency exposure on the GABAergic system in the rat cerebellum: clues from semi-quantitative immunohistochemistry. *Brain Res,* **912**, 33–46.

Meltz M L (2003). Radiofrequency exposure and mammalian cell toxicity, genotoxicity, and transformation. *Bioelectromagnetics,* **Suppl 6**, S196–213.

Mevissen M, Stamm A, Buntenkötter S, Zwingleberg R, Wahnschaffe U and Löscher W (1993). Effects of magnetic fields on mammary tumour development induced by 7,12-dimethylbenz(a)anthracene in rats, *Bioelectromagnetics,* **14**, 131–43.

Mevissen M, Buntenkotter S and Löscher W (1994). Effects of static and time-varying (50 Hz) magnetic fields on reproduction and fetal development in rats. *Teratology,* **50**(3), 229–37.

Mevissen M, Kietzmann M and Löscher W (1995). *In vivo* exposure of rats to a weak alternating magnetic field increases ornithine decarboxylase activity in the mammary gland by a similar extent as the carcinogen DMBA. *Cancer Lett,* **90**, 207–14.

Mevissen M, Lerchl A and Löscher W (1996a). Study on pineal function and DMBA-induced breast cancer formation in rats during exposure to a 100 mG, 50 Hz magnetic field. *J Toxicol Environ Health,* **48**(2),169–85.

Mevissen M, Lerchl A, Szamel M and Löscher W (1996b). Exposure of DMBA-treated female rats in a 50 Hz, 50 microTesla magnetic field: effects on mammary tumor growth, melatonin levels, and T lymphocyte activation. *Carcinogenesis,* **17**(5), 903–10.

Mevissen M, Haussler M, Lerchl A and Löscher W (1998a). Acceleration of mammary tumorigenesis by exposure of 7,12-dimethylbenz[a]anthracene-treated female rats in a 50 Hz, 100 μT magnetic field: replication study. *J Toxicol Environ Health A,* **53**(5), 401–18.

Mevissen M, Haussler M, Szamel M, Emmendorffer A, Thun-Battersby S and Löscher W (1998b). Complex effects of long-term 50 Hz magnetic field exposure *in vivo* on immune functions in female Sprague-Dawley rats depend on duration of exposure. *Bioelectromagnetics,* **19**(4), 259–70.

Mevissen M, Haussler M and Löscher W (1999). Alterations in ornithine decarboxylase activity in the rat mammary gland after different periods of 50 Hz magnetic field exposure. *Bioelectromagnetics,* **20**, 338–46.

Michael B D, Prise KM, Folkard M, Mitchell S and Gilchrist S (2004). Effects of 50 Hz EMF exposure on mammalian cells in culture. IN *Electromagnetic Enviroments and Health in Buildings* (D Clements-Croome, ed). London, Spon Press, pp 307–12.

Michelozzi P, Capon A, Kirchmayer U, Forastiere F, Biggeri A, Barca A and Perucci C A (2002). Adult and childhood leukemia near a high-power radio station in Rome, Italy. *Am J Epidemiol,* **155**, 1096–103.

Mickley G A, Cobb B L, Mason P A and Farrell S (1994). Disruption of a putative working memory task and selective expression of brain c-fos following microwave-induced hyperthermia. *Physiol Behav,* **55**, 1029–38.

Miller M W, Nyborg W L, Dewey W C, Edwards M J, Abramowicz J S and Brayman A A (2002). Hyperthermic teratogenicity, thermal dose and diagnostic ultrasound during pregnancy: implications of new standards on tissue heating. *Int J Hyperthermia,* **18**(5), 361–84.

Miller S C, Haberer J, Venkatachalam U and Furniss M J (1999). NF-kappaB or AP-1-dependent reporter gene expression is not altered in human U937 cells exposed to power-line frequency magnetic fields. *Radiat Res,* **151**(3), 310–18.

Milunsky A, Ulcickas M, Rothman K J, Willett W, Jick S S and Jick H (1992). Maternal heat exposure and neural tube defects. *J Am Med Assoc,* **268**, 882–5.

Miyakoshi J, Yamagishi N, Ohtsu S, Mohri K and Takebe H (1996a). Increase in hypoxanthine-guanine phosphoribosyl transferase gene mutations by exposure to high-density 50 Hz magnetic fields. *Mutat Res,* **349**(1), 109–14.

Miyakoshi J, Ohtsu S, Shibata T and Takebe H (1996b). Exposure to magnetic field (5 mT at 60 Hz) does not affect cell growth and c-myc gene expression. *J Radiat Res (Tokyo),* **37**(3), 185–91.

Miyakoshi J, Kitagawa K and Takebe H (1997). Mutation induction by high-density, 50 Hz magnetic fields in human MeWo cells exposed in the DNA synthesis phase. *Int J Radiat Biol,* **71**(1), 75–9.

Miyakoshi J, Koji Y, Wakasa T and Takebe H (1999). Long-term exposure to a magnetic field (5 mT at 60 Hz) increases X-ray-induced mutations. *J Radiat Res (Tokyo),* **40**(1), 13–21.

Miyakoshi J, Yoshida M, Yaguchi H and Ding G R (2000a). Exposure to extremely low frequency magnetic fields suppresses x-ray-induced transformation in mouse C3H10T1/2 cells. *Biochem Biophys Res Commun,* **271**(2), 323–7.

Miyakoshi J, Mori Y, Yaguchi H, Ding G and Fujimori A (2000b). Suppression of heat-induced HSP-70 by simultaneous exposure to 50 mT magnetic field. *Life Sci,* **66**(13), 1187–96.

Miyakoshi J, Yoshida M, Tarusawa Y, Nojima T, Wake K and Taki M (2001). Effects of high frequency electromagnetic fields on DNA damage using the Comet assay method. *Trans Inst Electr Eng (Jpn),* **121-A**, 1093–8.

Moen B E, Drablos P A, Pedersen S, Sjoen M and Thommesen G (1996). Absence of relation between sick leave caused by musculoskeletal disorders and exposure to magnetic fields in an aluminum plant. *Bioelectromagnetics,* **17**(1), 37–43.

Mokhtech K E, Delisle G Y and Roberge Andrée G (1994). SAR mapping within the human eye due to portable transceivers. IN Proceedings IEEE Symposium on Electromagnetic Compatibility, Chicago, 1994.

Moriarty L J and Borgens R B (2001). An oscillating extracellular voltage gradient reduces the density and influences the orientation of astrocytes in injured mammalian spinal cord. *J Neurocytol,* **30**, 45–57.

Morris J E, Sasser L B, Miller D L, Dagle G E, Rafferty C N, Ebi K L and Anderson L E (1999). Clinical progression of transplanted large granular lymphocytic leukemia in Fischer 344 rats exposed to 60 Hz magnetic fields. *Bioelectromagnetics,* **20**(1), 48–56.

Morrissey J J, Raney S, Heasley E, Rathina Velu P, Dauphinee M and Fallon J H (1999). Iridium exposure increase c-fos expression in the mouse brain only at the levels which likely result in tissue heating. *Neuroscience,* **92**, 1539–46.

Möse J R and Fischer G (1970). Zur Wirkung elektrostatischer Gleichfelder, weitere tierexperimentelle Ergebnisse. *Arch Hyg,* **154**, 378 (in German).

Mostafa R M, Mostafa Y M and Ennaceur A (2002). Effects of exposure to extremely low-frequency magnetic field of 2 G intensity on memory and corticosterone level in rats. *Physiol Behav,* **76**, 589–95.

Moulder J E, Erdreich L S, Malyapa R S, Merritt J, Pickard W F and Vijayalaxmi (1999). Cell phone and cancer: what is the evidence for a connection? *Radiat Res,* **151**, 513–31.

Mueller C H, Krueger H and Schierz C (2002). Project NEMESIS: perception of a 50 Hz electric and magnetic field at low intensities (laboratory experiment). *Bioelectromagnetics,* **23**(1), 26–36.

Mur J M, Wild P, Rapp R, Vautrin J P and Coulon J P (1998). Demographic evaluation of the fertility of aluminium industry workers: influence of exposure to heat and static magnetic fields. *Hum Reprod,* **13**(7), 2016–19.

Murakami J, Torii Y and Masuda K (1992). Fetal development of mice following intrauterine exposure to a static magnetic field of 6.3 T. *Magn Reson Imaging,* **10**(3), 433–7.

Murphy J C, Kaden D A, Warren J and Sivak A (1993). International Commission for Protection Against Environmental Mutagens and Carcinogens. Power frequency electric and magnetic fields: a review of genetic toxicology. *Mutat Res,* **296**(3), 221–40.

Murthy K K, Rogers W R and Smith H D (1995). Initial studies on the effects of combined 60 Hz electric and magnetic field exposure on the immune system of nonhuman primates. *Bioelectromagnetics,* **Suppl 3**, 93–102.

Muscat J E, Malkin M G, Shore R E, Thompson S, Neugut A I, Stellman S D and Bruce J (2002). Handheld cellular telephones and risk of acoustic neuroma. *Neurology,* **58**, 1304–6.

Muscat J E, Malkin M G, Thompson S, Shore R E, Stellman S D, McRee D, Neugut A I and Wynder E L (2000). Handheld cellular telephone use and risk of brain cancer. *J Am Med Assoc,* **284**, 3001–7. (Erratum in: *J Am Med Assoc,* **286**, 1293, 2001).

Nadel E R (1980). Circulatory and thermal regulations during exercise. *Fed Proc,* **39**, 1491–7.

Nadel E R (1984). Temperature regulation and hyperthermia during exercise. Symposium on exercise: physiology and clinical applications. *Clinics in Chest Medicine,* **5**(1), 13–20.

Nadel E R (1985). Recent advances in temperature regulation during exercise in humans. *Fed Proc,* **44**(7), 2286–92.

Nafziger J, Desjobert H, Benamar B, Guillosson J J and Adolphe M (1993). DNA mutations and 50 Hz electromagnetic fields. *Bioelectrochem Bioenerg,* **30**, 130–41.

Narita K, Hanakawa K, Kasahara T, Hisamitsu T and Asano K (1997). Induction of apoptotic cell death in human leukemic cell line, HL-60, by extremely low frequency electric magnetic fields: analysis of the possible mechanisms *in vitro*. *In Vivo,* **11**, 329–35.

Narra V R, Howell R W, Goddu S M and Rao D V (1996). Effects of a 1.5-tesla static magnetic field on spermatogenesis and embryogenesis in mice. *Invest Radiol,* **31**(9), 586–90.

Natarajan M, Vijayalaxmi, Szzliagyl M, Roldan F N and Meltz M L (2002). NF-kappaB DNA-binding activity after high peak power pulsed microwave (8.2 GHz) exposure of normal human monocytes. *Bioelectromagnetics,* **23**, 271–7.

NCRP (1986). Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields. Bethesda MD, National Council on Radiation Protection and Measurements, NCRP Report No. 86.

Nelson B K, Conover D L, Shaw P B, Snyder D L and Edwards R M (1997a). Interactions of radiofrequency radiation on 2-methoxyethanol teratogenicity in rats. *J Appl Toxicol,* **17**, 31–9.

Nelson B K, Conover D L, Krieg E F Jr, Snyder D L and Edwards R M (1997b). Interactions of radiofrequency radiation-induced hyperthermia and 2-methoxyethanol teratogenicity in rats. *Bioelectromagnetics,* **18**, 349–59.

Nelson B K, Snyder D L and Shaw P B (1999). Developmental toxicity interactions of salicylic acid and radiofrequency radiation or 2-methoxyethanol in rats. *Reprod Toxicol,* **13**, 137–45.

Nelson B K, Snyder D L and Shaw P B (2001). Developmental toxicity interactions of methanol and radiofrequency radiation or 2-methoxyethanol in rats. *Int J Toxicol*, **20**, 89–100.

Neubauer C, Phelan, A M, Kues H and Lange D G (1990). Microwave irradiation of rats at 2.45 GHz activates pinocytotic-like uptake of tracer by capillary endothelial cells of cerebral cortex. *Bioelectromagnetics*, **11**, 261–8.

Neutra R R, DelPizzo V and Lee G M (2002). An evaluation of the possible risks from electric and magnetic fields (EMFs) from power lines, internal wiring, electrical occupations, and appliances. Final report, June 2002. California EMF Program, Oakland, USA. http://www.dhs.ca.gov/ehib/emf/RiskEvaluation/riskeval.html.

Nguyen P, Bournias-Vardiabasis N, Haggren W, Adey W R and Phillips J L (1995). Exposure of *Drosophila melanogaster* embryonic cell cultures to 60 Hz sinusoidal magnetic fields: assessment of potential teratogenic effects. *Teratology*, **51**(4), 273–7.

Niehaus M, Bruggemeyer H, Behre H M and Lerchl A (1997). Growth retardation, testicular stimulation, and increased melatonin synthesis by weak magnetic fields (50 Hz) in Djungarian hamsters, *Phodopus sungorus*. *Biochem Biophys Res Commun*, **234**(3), 707–11.

NIEHS (1998). National Institute of Enviromental Health Sciences working group report. Assessment of Health Effects from Exposure to Power-line Frequency Electric and Magnetic Fields (C J Portier and M S Wolfe). Research Triangle Park NC, National Institute of Health, NIH Publication No 98-3981.

NIEHS (1999). National Institute of Enviromental Health Sciences report. Health Effects from Exposure to Powerline Frequency Electric and Magnetic Fields. Research Triangle Park NC, National Institute of Health, NIH Publication No 99-4493.

Nilius B and Droogmans G (2001). Ion channels and their role in vascular endothelium. *Physiol Rev*, **81**(4), 1415–59.

Nindl G, Swez J A, Miller J M and Balcavage W X (1997). Growth stage dependent effects of electromagnetic fields on DNA synthesis of Jurkat cells. *FEBS Lett*, **414**(3), 501–6.

NIOSH (1972). National Institute for Occupational Safety and Health. Criteria for a Recommeded Standard – Occupational Exposure to Hot Environments. Washington DC, US Government Printing Office, Publication No. 72-10269.

NIOSH (1980). Proceedings NIOSH Workshop on Recommended Heat Stress Standards (F N Dukes-Dubos and A Henschel, eds). Cincinnati, Ohio, US Department of Health and Human Services, DHHS (NIOSH) 81.

NIOSH (1986). Criteria for a Recommended Standard. Occupational Exposure to Hot Environments Revised Criteria 1986. US Department of Health and Human Services, DHHS (NIOSH) 86-113.

Nolte C M, Pittman D W, Kalevitch B, Henderson R and Smith J C (1998). Magnetic field conditioned taste aversion in rats. *Physiol Behav*, **63**(4), 683–8.

Nordenson I, Mild K H, Andersson G and Sandström M (1994). Chromosomal aberrations in human amniotic cells after intermittent exposure to fifty hertz magnetic fields. *Bioelectromagnetics*, **15**(4), 293–301.

Novoselova E G, Fesenko E E, Makar V R and Sadovnikov V B (1999). Microwaves and cellular immunity: II. Immunostimulating effects of microwaves and naturally occurring antioxidant nutrients. *Bioelectrochem Bioenerg*, **49**(1), 37–41.

Novoselova E G, Ogai V B, Sorokina O V, Novikov V V and Fesenko E E (2001). Effect of centimeter microwaves and the combined magnetic field on the tumor necrosis factor production in cells of mice with experimental tumors. *Biofizika*, **46**(1), 131–5.

NRC (1997). Possible Health Effects of Exposure to Residential Electric and Magnetic Fields. National Research Council (US) Committee on the Possible Effects of Electromagnetic Fields on Biologic Systems. Washington, National Academy Press.

NRPB (1993). Restrictions on human exposure to static and time varying electromagnetic fields and radiation: scientific basis and recommendations for the implementation of the Board's Statement. *Doc NRPB*, **4**(5), 7–63.

NRPB (1995). Risk of radiation-induced cancer at low doses and low dose rates for radiation protection purposes. *Doc NRPB*, **6**(1), 1–77.

NRPB (1999). Advice on the 1998 ICNIRP guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz). *Doc NRPB*, **10**(2), 1–59.

NRPB (2000). Minutes of the Board Meeting held on Thursday 25 May 2000, Item 1(1). http://www.nrpb.org/about_us/the_board/minutes_of_meetings/25may00.pdf.

NTP (1999a). National Toxicology Program technical report. Toxicology and carcinogenesis studies of 60 Hz magnetic fields in F344/N rats and B6C3F1 mice. Washington DC, NTPTR 488, NIH Publication No. 99-3978.

NTP (1999b). National Toxicology Program technical report. Studies of magnetic field promotion (DMBA initiation) in Sprague-Dawley rats (gavage/whole-body exposure studies). Washington DC, NTPTR 489, NIH Publication No. 99-3979.

Nuccitelli R (1992). Endogenous ionic currents and DC electric fields in multicellular animal tissues. *Bioelectromagnetics*, **Suppl 1**, 147–57.

Nuccitelli R (2003). Endogenous electric fields in embryos during development, regeneration and wound healing. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim*, **106**(4), 375–84.

Nyenhuis J A, Bourland J D, Kildishev A V and Schaefer D J (2001). Health effects and safety of intense gradient fields. IN *Magnetic Resonance Procedures: Health Effects and Safety* (F Shellock, ed). Boca Raton, CRC Press, pp 31–54.

O'Connor M E (1999). Intrauterine effects in animals exposed to radiofrequency and microwave fields. *Teratology*, **59**, 287–91.

Ogiue-Ikeda M, Kotani H and Iwasaka M (2001). Inhibition of leukemia cell growth under magnetic fields of up to 8 T. *IEEE Trans Magn*, **37**(4), 2912–14.

Ohkubo C and Xu S (1997). Acute effects of static magnetic fields on cutaneous microcirculation in rabbits. *In Vivo*, **11**(3), 221–5.

Okano H and Ohkubo C (2001). Modulatory effects of static magnetic fields on blood pressure in rabbits. *Bioelectromagnetics*, **22**(6), 408–18.

Okano H, Gmitrov J and Ohkubo C (1999). Biphasic effects of static magnetic fields on cutaneous microcirculation in rabbits. *Bioelectromagnetics*, **20**(3), 161–71.

Okoniewski M and Stuchly M A (1996). A study of the handset antenna and human body interaction. *IEEE Trans Microwave Theory Techniq*, **44**, 1855–64.

Okonogi H, Nakagawa M and Tsuji Y (1996). The effects of a 4.7 tesla static magnetic field on the frequency of micronucleated cells induced by mitomycin C. *Tohoku J Exp Med*, **180**(3), 209–15.

Oppenheimer M and Preston-Martin S (2002). Adult onset acute myelogenous leukemia and electromagnetic fields in Los Angeles County: bed-heating and occupational exposures. *Bioelectromagnetics*, **23**, 411–15.

Orcutt N and Gandhi O P (1988). A 3-D impedance method to calculate power deposition in biological materials subjected to time varying magnetic fields. *IEEE Trans Biomed Eng*, **35**, 577–83.

Orr J L, Rogers W R and Smith H D (1995a). Detection thresholds for 60 Hz electric fields by nonhuman primates. *Bioelectromagnetics*, **3**, 23–34.

Orr J L, Rogers W R and Smith H D (1995b). Exposure of baboons to combined 60 Hz electric and magnetic fields does not produce work stoppage or affect operant performance on a match-to-sample task. *Bioelectromagnetics*, **3**, 61–70.

Osbakken M, Griffith J and Taczanowsky P (1986). A gross morphologic, histologic, hematologic, and blood chemistry study of adult and neonatal mice chronically exposed to high magnetic fields. *Magn Reson Med*, **3**(4), 502–17.

Pacini S, Vannelli G B, Barni T, Ruggiero M, Sardi I, Pacini P and Gulisano M (1999a). Effect of 0.2 T static magnetic field on human neurons: remodeling and inhibition of signal transduction without genome instability. *Neurosci Lett*, **267**(3), 185–8.

Pacini S, Aterini S, Pacini P, Ruggiero C, Gulisano M and Ruggiero M (1999b). Influence of static magnetic field on the antiproliferative effects of vitamin D on human breast cancer cells. *Oncol Res*, **11**(6), 265–71.

Pafkova H and Jerabek J (1994). Interaction of MF 50 Hz, 10 mT with high dose of X-rays: evaluation of embryotoxicity in chick embryos. *Rev Environ Health*, **10**(3–4), 235–41.

Pafkova H, Jerabek J, Tejnorova I and Bednar V (1996). Developmental effects of magnetic field (50 Hz) in combination with ionizing radiation and chemical teratogens. *Toxicol Lett*, **88**(1–3), 313–16.

Paile W, Jokela K, Koivistoinen A and Salomaa S (1995). Effects of 50 Hz sinusoidal magnetic fields and spark discharges on human lymphocytes *in vitro*. *Bioelectrochem Bioenerg,* **36**, 15–22.

Pakhomov A G, Akyel Y, Pakhomova O N, Stuck B E and Murphy M R (1998). Current state and implications of research on biological effects of millimeter waves: a review of the literature. *Bioelectromagnetics,* **19**, 393–413.

Pakhomova O N, Belt M L, Mathur S P, Lee J C and Akyel Y (1997). Lack of genetic effects of ultrawide-band electromagnetic radiation in yeast. *Electro- Magnetobiol,* **16**, 195–201.

Parker J E and Winters W (1992). Expression of gene-specific RNA in cultured cells exposed to rotating 60 Hz magnetic fields. *Biochem Cell Biol,* **70**(3–4), 237–41.

Parpura V, Basarsky TA, Liu F, Jeftinija K, Jeftinija S and Haydon PG (1994). Glutamate-mediated astrocyte-neuron signalling. *Nature,* **369**(6483), 744–7.

Pashovkina M S and Akoev I G (2000). Changes in serum alkaline phosphatase activity during *in vitro* exposure to amplitude-modulated electromagnetic field of ultrahigh frequency (2375 MHz) in guinea pigs. *Biofizika,* **45**, 130–36.

Paul M E (1993). Physical agents in the workplace. *Seminars in Perinatology,* **17**, 5–17.

Penafiel L M, Litovitz T, Krause D, Desta A and Mullins J M (1997). Role of modulation on the effect of microwaves on ornithine decarboxylase activity in L929 cells. *Bioelectromagnetics,* **18**, 132–41.

Pennes H H (1948). Analysis of tissue and arterial blood temperature in the resting human forearm. *J Appl Physiol,* **1**, 93–122.

Persson B R R, Salford, L G and Brun A (1997). Blood–brain barrier permeability in rats exposed to electromagnetic fields used in wireless communication. *Wireless Networks,* **3**, 455–61.

Peyman A, Rezazadeh A A and Gabriel C (2001). Changes in the dielectric properties of rat tissue as a function of age at microwave frequencies. *Phys Med Biol,* **46**(6).

Pfluger D H and Minder C E (1996). Effects of exposure to 16.7 Hz magnetic fields on urinary 6-hydroxymelatonin sulfate excretion of Swiss railway workers. *J Pineal Res,* **21**, 91–100.

Phillips J L, Haggren W, Thomas W J, Ishida-Jones T and Adey W R (1992). Magnetic field-induced changes in specific gene transcription. *Biochim Biophys Acta,* **1132**(2), 140–44.

Pipkin J L, Hinson W G, Young J F, Rowland K L, Shaddock J G, Tolleson W H, Duffy P H and Casciano D A (1999). Induction of stress proteins by electromagnetic fields in cultured HL-60 cells. *Bioelectromagnetics,* **20**(6), 347–57.

Pirhonen J P, Vähä-Eskeli K K, Seppänen A, Vuorinen J and Erkkola R U (1994). Does thermal stress decrease uterine blood flow in hypertensive pregnancies? *Am J Perinatol,* **11**, 313–16.

Podd J V, Whittington C J, Barnes G R, Page W H and Rapley B I (1995). Do ELF magnetic fields affect human reaction time? *Bioelectromagnetics,* **16**(5), 317–23.

Podd J, Abbott J, Kazantzis N and Rowland A (2002). Brief exposure to a 50 Hz, 100 μT magnetic field: effects on reaction time, accuracy, and recognition memory. *Bioelectromagnetics,* **23**, 189–95.

Potschka H, Thun-Battersby S and Löscher W (1998). Effect of low-intensity 50 Hz magnetic fields on kindling acquisition and fully kindled seizures in rats. *Brain Res,* **809**(2), 269–76.

Power G G (1989). Biology of temperature: the mammalian fetus. *J Devel Physiol,* **12**, 295–304.

Prasad A V, Miller M W, Carstensen E L, Cox C, Azadniv M and Brayman A A (1991). Failure to reproduce increased calcium uptake in human lymphocytes at purported cyclotron resonance exposure conditions. *Radiat Environ Biophys,* **30**(4), 305–20.

Prato F S, Wills J M, Roger J, Frappier H, Drost D J, Lee T Y, Shivers R R and Zabel P (1994). Blood–brain barrier permeability in rats is altered by exposure to magnetic fields associated with magnetic resonance imaging at 1.5 T. *Microsc Res Tech,* **27**(6), 528–34.

Prato F S, Carson J J, Ossenkopp K P and Kavaliers M (1995). Possible mechanisms by which extremely low frequency magnetic fields affect opioid function. *FASEB J,* **9**(9), 807–14.

Prato F S, Kavaliers M and Carson J J (1996). Behavioural response to magnetic fields by land snails are dependent on both magnetic field direction and light. *Proc Roy Soc Lond B,* **263**, 1437–42.

Prato F S, Kavaliers M, Cullen AP and Thomas A W (1997). Light-dependent and -independent behavioral effects of extremely low frequency magnetic fields in a land snail are consistent with a parametric resonance mechanism. *Bioelectromagnetics,* **18**(3), 284–91.

Prato F S, Kavaliers M and Thomas A W (2000). Extremely low frequency magnetic fields can either increase or decrease analgaesia in the land snail depending on field and light conditions. *Bioelectromagnetics,* **21**(4), 287–301.

Preece A W, Wesnes K A and Iwi G R (1998). The effect of a 50 Hz magnetic field on cognitive function in humans. *Int J Radiat Biol,* **74**(4), 463–70.

Preece A W, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E and Varey A (1999). Effect of a 915 MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol,* **75**(4), 447–56.

Pu J S, Chen J, Yang Y H and Bai Y Q (1997). The effects of 3000 MHz microwave irradiation on electroencephalic energy and energy metabolism in mouse brain. *Electro- Magnetobiol,* **16**, 243–7.

Radon K, Parera D, Rose D M, Jung D and Vollrath L (2001). No effects of pulsed radio frequency electromagnetic fields on melatonin, cortisol, and selected markers of the immune system in man. *Bioelectromagnetics,* **22**(4), 280–87.

Ramsey J D, Burford C L, Beshir M Y, and Jensen R C (1983). Effects of workplace thermal conditions on safe work behaviour. *J Saf Res,* **14**, 105–14.

Rannug A, Ekstrom T, Mild K H, Holmberg B, Gimenez-Conti I and Slaga T J (1993a). A study on skin tumour formation in mice with 50 Hz magnetic field exposure. *Carcinogenesis,* **14**(4), 573–8.

Rannug A, Holmberg B and Mild K H (1993b). A rat liver foci promotion study with 50 Hz magnetic fields. *Environ Res,* **62**(2), 223–9.

Rannug A, Holmberg B, Ekstrom T and Mild K H (1993c). Rat liver foci study on coexposure with 50 Hz magnetic fields and known carcinogens. *Bioelectromagnetics,* **14**(1), 17–27.

Rannug A, Holmberg B, Ekstrom T, Mild K H, Gimenez-Conti I and Slaga T J (1994). Intermittent 50 Hz magnetic field and skin tumor promotion in SENCAR mice. *Carcinogenesis,* **15**(2), 153–7.

Raylman R R, Clavo A C and Wahl R L (1996). Exposure to strong static magnetic field slows the growth of human cancer cells *in vitro*. *Bioelectromagnetics,* **17**(5), 358–63.

Rea W J, Pan Y, Fenyves E J, Sujisawa I, Samadi N and Ross G H (1991). Electromagnetic field sensitivity. *J Biol,* **10**, 241–56.

Reid S W and Gettinby G (1998). Radio-frequency electromagnetic field from mobile phones. *Lancet,* **352**(9127), 576–7.

Reilly J P (1998). Cardiac sensitivity to stimulation. IN *Applied Bioelectricity: From Electrical Stimulation to Electropathology* (J P Reilly, ed). New York, Springer, Chapter 6, pp 194–239.

Reilly J P (1999). Electrophysiology in the zero to MHz range as a basis for electric and magnetic field *exposure standards*. IN *Health Effects of Electromagnetic Fields in the Frequency Range 300 Hz to 10 MHz (*R Matthes, E van Rongen and M H Repacholi, eds). München, Märkel-Druck, ICNIRP 8/99, pp 69–104.

Reilly J P (2002). Neuroelectric mechanisms applied to low frequency electric and magnetic field exposure guidelines – part 1: sinusoidal waveforms. *Health Phys,* **83**(3), 341–55.

Reipert B M, Allan D and Dexter T M (1996). Exposure to extremely low frequency magnetic fields has no effect on growth rate or clonogenic potential of multipotential haemopoietic progenitor cells. *Growth Factors,* **13**(3–4), 205–17.

Reipert B M, Allan D, Dale R E and Dexter T M (1994). Interaction of low frequency, low intensity electromagnetic fields with haemopoetic stem cells. IN Abstracts, 16th Annual Meeting of the Bioelectromagnetics Society, Copenhagen, June 1994.

Reipert B M, Allan D, Reipert S and Dexter T M (1997). Apoptosis in haemopoietic progenitor cells exposed to extremely low-frequency magnetic fields. *Life Sci,* **61**(16), 1571–82.

Reiter R J (1980). The pineal and its hormones in the control of reproduction in mammels. *Endocrine Rev,* **1**, 109–31.

Reiter R J (1993). Static and extremely low frequency electromagnetic field exposure: reported effects on the circadian production of melatonin. *J Cell Biochem,* **51**(4), 394–403.

Reiter R J, Anderson L E, Buschbom R L and Wilson B W (1988). Reduction of the nocturnal rise in pineal melatonin levels in rats exposed to 60 Hz electric fields *in utero* and for 23 days after birth. *Life Sci,* **42**(22), 2203–6.

Repacholi M H (1998). Low level exposure to radiofrequency electromagnetic fields: health effects and research needs. *Bioelectromagnetics,* **19**, 1–19.

Repacholi M H and Cardis E (1997). Criteria for health risk assessment. *Radiat Prot Dosim,* **72**(3–4), 305–12.

Repacholi M H and Greenebaum B (1999). Interaction of static and extremely low frequency electric and magnetic fields with living systems: health effects and research needs. *Bioelectromagnetics,* **20**(3), 133–60.

Repacholi M H, Basten A, Gebski V, Noonan D, Finnie J and Harris A W (1997). Lymphomas in Eμ-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields. *Radiat Res,* **147**, 631–40.

Riu P J, Foster K R, Blick W and Adair E R (1997). A thermal model for human thresholds of microwave-evoked warmth sensations. *Bioelectromagnetics,* **18**, 578–83.

Rogers W R, Reiter R J, Smith H D and Barlow-Walden L (1995a). Rapid-onset/offset, variably scheduled 60 Hz electric and magnetic field exposure reduces nocturnal serum melatonin concentration in nonhuman primates. *Bioelectromagnetics,* **Suppl 3**, 119–22.

Rogers W R, Reiter R J, Barlow-Walden L, Smith H D and Orr J L (1995b). Regularly scheduled, day-time, slow-onset 60 Hz electric and magnetic field exposure does not depress serum melatonin concentration in nonhuman primates. *Bioelectromagnetics,* **Suppl 3**, 111–18.

Rommereim D N, Rommereim R L, Miller D L, Buschbom R L and Anderson L E (1996). Developmental toxicology evaluation of 60 Hz horizontal magnetic fields in rats. *Appl Occup Environ Hyg,* **11**, 307–12.

Ronneberg A, Haldorsen T, Romundstad P, Andersen A (1999). Occupational exposure and cancer incidence among workers from an aluminum smelter in western Norway. *Scand J Work Environ Health,* **25**(3), 207–14.

Rooke G A, Savage M V and Brengelmann G L (1994). Maximal skin blood flow is decreased in elderly men. *J Appl Physiol,* **77**(1), 11–14.

Roschke J and Mann K (1997). No short-term effects of digital mobile radio telephone on the awake human electroencephalogram. *Bioelectromagnetics,* **18**(2), 172–6.

Rosen A D (1996). Inhibition of calcium channel activation in GH3 cells by static magnetic fields. *Biochim Biophys Acta,* **1282**(1), 149–55.

Ross J (2000). Dietary flavonoids and the MLL gene: a pathway to infant leukaemia? *Proc Natl Acad Sci (USA),* **97**, 4411–13.

Ross J A, Potter J D, Reaman G H, Pendergrass T W and Robison L (1996). Maternal exposure to potential inhibitors of DNA topoisomerase II and infant leukaemia (United States): a report from the Childrens Cancer Group. *Cancer Causes Control,* **7**, 581–90.

Roti Roti J L, Malyapa R S, Bisht K S, Ahern E W, Moros E G, Pickard W F and Straube W L (2001). Neoplastic transformation in C3H 10T(1/2) cells after exposure to 835.62 MHz FDMA and 847.74 MHz CDMA radiations. *Radiat Res,* **155**(1 Part 2), 239–47.

Rowell L B (1983). Cardiovascular aspects of human thermoregulation. *Circ Res,* **52**, 367–79.

Ryan B M, Mallett E Jr, Johnson T R, Gauger J R and McCormick D L (1996). Developmental toxicity study of 60 Hz (power frequency) magnetic fields in rats. *Teratology,* **54**(2), 73–83.

Ryan B M, Symanski R R, Pomeranz L E, Johnson T R, Gauger J R and McCormick D L (1999). Multigeneration reproductive toxicity assessment of 60 Hz magnetic fields using a continuous breeding protocol in rats. *Teratology,* **59**(3), 156–62.

Ryan B M, Polen M, Gauger J R, Mallett E Jr, Kearns M B, Bryan T L and McCormick D L (2000). Evaluation of the developmental toxicity of 60 Hz magnetic fields and harmonic frequencies in Sprague-Dawley rats. *Radiat Res,* **153**(5 Part 2), 637–41.

Sabo J, Mirossay L, Horovcak L, Sarissky M, Mirossay A and Mojzis J (2002). Effects of static magnetic field on human leukemic cell line HL-60. *Bioelectrochemistry,* **56**(1–2), 227–31.

Saffer J D and Thurston S J (1995). Short exposures to 60 Hz magnetic fields do not alter MYC expression in HL60 or Daudi cells. *Radiat Res,* **144**(1), 18–25.

Saffer J D, Chen G, Colburn N H and Thurston S J (1997). Power frequency magnetic fields do not contribute to transformation of JB6 cells. *Carcinogenesis,* **18**(7), 1365–70.

Sahl J, Mezei G, Kavet, R et al (2002). Occupational magnetic field exposure and cardiovascular mortality in a cohort of electric utility workers. *Am J Epidemiol,* **156**, 913–18.

Saito K, Saiga T and Suzuki K (1998). Reversible irritative effect of acute 2.45 GHz microwave exposure on rabbit eyes – a preliminary evaluation. *J Toxicol Sci,* **23**, 197–203.

Sakamoto S, Hagino N and Winters W D (1993). In vivo studies of the effect of magnetic field exposure on ontogeny of choline acetyltransferase in the rat brain. *Bioelectromagnetics,* **14**(4), 373–81.

Salerno S, Lo Casto A, Caccamo N, d'Anna C, de Maria M, Lagalla R, Scola L and Cardinale A E (1999). Static magnetic fields generated by a 0.5 T MRI unit affects *in vitro* expression of activation markers and interleukin release in human peripheral blood mononuclear cells (PBMC). *Int J Radiat Biol,* **75**(4), 457–63.

Salford L G, Brun A and Persson B R R (1997). Brain tumour development in rats exposed to electromagnetic fields used in wireless cellular communication. *Wireless Networks,* **3**, 463–9.

Salford L G, Brun A E, Eberhardt J L, Malmgren L and Persson B R (2003). Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones. *Environ Health Perspect,* **111**(7), 881–3.

Sandstrom M, Lyskov E, Berglund A, Medvedev S and Mild K H (1997). Neurophysiological effects of flickering light in patients with perceived electrical hypersensitivity. *J Occup Environ Med,* **39**(1), 15–22.

Sandström M, Wilen J, Oftedal G and Hansson Mild K (2001). Mobile phone use and subjective symptoms. Comparison of symptoms experienced by users of analogue and digital mobile phones. *Occup Med (Lond),* **51**(1), 25–35.

Santini R, Hosni M, Deschaux P and Pacheco H (1988). B16 melanoma development in black mice exposed to low-level microwave radiation. *Bioelectromagnetics,* **9**, 105–7.

Santini R, Santini P, Danze J M, Le Ruz P and Seigne M (2003). Symptoms experienced by people in vicinity of base stations: II/ Incidences of age, duration of exposure, location of subjects in relation to the antennas and other electromagnetic factors. *Pathol Biol (Paris),* **51**(7), 412–15.

Santoro N, Lisi A, Pozzi D, Pasquali E, Serafino A and Grimaldi S (1997). Effect of extremely low frequency (ELF) magnetic field exposure on morphological and biophysical properties of human lymphoid cell line (Raji). *Biochim Biophys Acta,* **1357**(3), 281–90.

Sarkar S, Ali S and Behari J (1994). Effect of low power microwave on the mouse genome: a direct DNA analysis. *Mutat Res,* **320**, 141–7.

Sartucci F, Bonfiglio L, Del Seppia C, Luschi P, Ghione S, Murri L and Papi F (1997). Changes in pain perception and pain-related somatosensory evoked potentials in humans produced by exposure to oscillating magnetic fields. *Brain Res,* **769**(2), 362–6.

Sasser L B, Anderson L E, Morris J E, Miller D L, Walborg E F Jr, Kavet R, Johnston D A and DiGiovanni J (1998). Lack of a co-promoting effect of a 60 Hz magnetic field on skin tumorigenesis in SENCAR mice. *Carcinogenesis,* **19**(9), 1617–21.

Sasser L B, Morris J E, Miller D L, Rafferty C N, Ebi K L and Anderson L E (1996). Exposure to 60 Hz magnetic fields does not alter clinical progression of LGL leukemia in Fischer rats. *Carcinogenesis,* **17**(12), 2681–7.

Sasser L B, Morrisd J E, Buschborn R L, Miller D L and Anderson L E (1991). Effect of 60 Hz electric fields on pienal melatonin during various times of the dark period. IN Project resumes, DOE Annual review of research on biological effects of 50 and 60 Hz electric and magnetic fields, November 1991. Milwaukee, Wisconsin, pA-24.

Sastre A, Cook M R and Graham C (1998). Nocturnal exposure to intermittent 60 Hz magnetic fields alters human cardiac rhythm. *Bioelectromagnetics,* **19**(2), 98–106.

Sastre A, Graham C and Cook M R (2000). Brain frequency magnetic fields alter cardiac autonomic control mechanisms. *Clin Neurophysiol,* **111**(11), 1942–8.

Sauer H, Hescheler J, Reis D, Diedershagen H, Niedermeier W and Wartenberg M (1997). DC electrical field-induced c-fos expression and growth stimulation in multicellular prostate cancer spheroids. *Br J Cancer,* **75**(10), 1481–8.

Saunders R D (2003). Rapporteur report: weak field interactions in the central nervous system. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 357–62.

Saunders R D and Jefferys J G R (2002). Weak electric field interactions in the central nervous system. *Health Phys,* **83**(3), 366–75.

Saunders R D, Cridland N A, Kowalczuk C I and Sienkiewicz Z J (1997). *In vivo* biological studies relevant to low level RF health effects. IN *Non-thermal Effects of RF Electromagnetic Fields* (J H Bernhardt, R Matthes and M H Repacholi, eds). München, ICNIRP, pp 145–61.

Saunders R D, Kowalczuk C I and Sienkiewicz Z J (1991). Biological effects of exposure to non-ionising electromagnetic fields and radiation. Chilton, NRPB-R240.

Scarfi M R, Lioi M B, Zeni O, Franceschetti G, Franceschi C and Bersani F (1994). Lack of chromosomal aberration and micronucleus induction in human lymphocytes exposed to pulsed magnetic fields. *Mutat Res*, **306**(2), 129–33.

Scarfi M R, Lioi M B, d'Ambrosio G, Massa R, Zeni O, Di Pietro R and Di Berardino D (1996). Genotoxic effects of mitomycin-C and microwave radiation on bovine lymphocytes. *Electro- Magnetobiol*, **15**, 99–107.

Schenck J F, Dumoulin C L, Redington R W, Kressel H Y, Elliott R T and McDougall I L (1992). Human exposure to 4.0-tesla magnetic fields in a whole-body scanner. *Med Phys*, **19**, 1089–98.

Schienle A, Stark R, Kulzer R, Klopper R and Vaitl D (1996). Atmospheric electromagnetism: individual differences in brain electrical response to simulated sferics. *Int J Psychophysiol*, **21**(2–3), 177–88.

Schimmelpfeng J and Dertinger H (1993). The action of 50 Hz magnetic and electric fields upon cell proliferation and cyclic AMP content of cultured mammalian cells. *J Bioelectrochem Bioenerg*, **30**, 143–50.

Schimmelpfeng J and Dertinger H (1997). Action of a 50 Hz magnetic field on proliferation of cells in culture. *Bioelectromagnetics*, **18**(2), 177–83.

Schneider T, Thalau H P and Semm P (1994). Effects of light or different earth-strength magnetic fields on the nocturnal melatonin concentration in a migratory bird. *Neurosci Lett*, **168**(1–2), 73–5.

Schoenfeld E R, O'Leary E S, Henderson K, Grimson R, Kabat G C, Ahnn S, Kaune W T, Gammon M D and Leske M C (2003). Electromagnetic fields and breast cancer on Long Island: a case–control study. *Am J Epidemiol*, **158**, 47–58.

Schonborn F, Burkhardt M and Kuster N (1998). Differences in energy absorption between heads of adults and children in the near fields of sources. *Health Phys*, **74**, 160–68.

Schreiber W G, Teichmann E M, Schiffer I, Hast J, Akbari W, Georgi H, Graf R, Hehn M, Spiebeta H W, Thelen M, Oesch F and Hengstler J G (2001). Lack of mutagenic and co-mutagenic effects of magnetic fields during magnetic resonance imaging. *J Magn Reson Imaging*, **14**(6), 779–88.

Schröder H J and Power G G (1997). Engine and radiator: fetal and placental interactions for heat dissipation. *Exp Physiol*, **82**, 403–14.

Schwartz J-L (1978). Influence of a constant magnetic field on nervous tissues: I. Nerve conduction velocity studies. *IEEE Trans Biomed Eng*, **25**, 467.

Schwartz J-L (1979). Influence of a constant magnetic field on nervous tissues: II. Voltage-clamp studies. *IEEE Trans Biomed Eng*, **26**, 238.

Schwartz J-L and Crooks L E (1982). NMR imaging produces no observable mutations or cytotoxicity in mammalian cells. *Am J Radiol*, **139**, 583.

SCST (1999). Science and Technology Committee Third Report. Scientific advisory system: mobile phones and health. Volume 1, Report and Proceedings of the Committee. http://www.parliament.the-stationery-office.co.uk/pa/cm199899/cmselect/cmsctech/489/48902.htm.

Seaman R L, Parker J E, Kiel J L, Mathur S P, Grubbs T R and Prol H K (2002). Ultra-wideband pulses increase nitric oxide production by RAW 264.7 macrophages incubated in nitrate. *Bioelectromagnetics*, **23**, 83–7.

Selmaoui B and Touitou Y (1995). Sinusoidal 50 Hz magnetic fields depress rat pineal NAT activity and serum melatonin. Role of duration and intensity of exposure. *Life Sci*, **57**(14), 1351–8.

Selmaoui B, Bogdan A, Auzeby A, Lambrozo J and Touitou Y (1996). Acute exposure to 50 Hz magnetic field does not affect hematologic or immunologic functions in healthy young men: a circadian study. *Bioelectromagnetics*, **17**(5), 364–72.

Selmaoui B, Lambrozo J and Touitou Y (1997). Endocrine functions in young men exposed for one night to a 50 Hz magnetic field. A circadian study of pituitary, thyroid and adrenocortical hormones. *Life Sci*, **61**(5), 473–86.

Sharma H S and Hoopes P J (2003). Hyperthermia-induced pathophysiology of the central nervous system. IN Proceedings of a WHO Workshop on Adverse Temperature Levels in the Human Body, Geneva, March 2002. *Int J Hyperthermia,* **19**(3), 325–55.

Shellock F G (ed) (2001). *Magnetic Resonance Procedures: Health Effects and Safety.* Boca Raton, CRC Press.

Shellock F G, Schaefer D J and Crues J V (1989). Alterations in body and skin temperatures caused by magnetic resonance imaging: is the recommended exposure for radiofrequency radiation too conservative? *Br J Radiol,* **62**, 904–9.

Shellock F G, Schaefer D J and Kanal E (1994). Physiologic responses to an MR imaging procedure performed at a specific energy absorption rate of 6.0 W/kg. *Radiology,* **192**, 865–8.

Shen Y H, Shao B J, Chiang H, Fu Y D and Yu M (1997). The effects of 50 Hz magnetic field exposure on dimethylbenz(alpha)anthracene induced thymic lymphoma/leukemia in mice. *Bioelectromagnetics,* **18**(5), 360–64.

Sheppard A R, Kavet R and Renew D C (2002). Exposure guidelines for low-frequency electric and magnetic fields: report from the Brussels Workshop. *Health Phys,* **83**(3), 324–32.

Sienkiewicz Z (2002). Biological effects of microwaves: animal studies. IN *The Review of Radio Science 1999–2002* (W Ross Stone and P Wilkinson, eds). IEEE Press/Wiley, pp 943–64.

Sienkiewicz Z J (2003). Rapporteur report: other tissues. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 391–6.

Sienkiewicz Z J, Saunders R D and Kowalczuk C I (1991). Biological effects of exposure to non-ionising electromagnetic fields and radiations: II. Extremely low frequency electric and magnetic fields. Chilton, NRPB-R239.

Sienkiewicz Z J, Cridland N A, Kowalczuk C I and Saunders R D (1993). Biological effects of electromagnetic fields and radiation. IN *The Review of Radio Science 1990–1992* (W R Stone, ed). New York, Oxford University Press, p 737.

Sienkiewicz Z J, Robbins L, Haylock R G and Saunders R D (1994). Effects of prenatal exposure to 50 Hz magnetic fields on development in mice: II. Postnatal development and behavior. *Bioelectromagnetics,* **15**(4), 363–75.

Sienkiewicz Z J, Larder S and Saunders R D (1996a). Prenatal exposure to a 50 Hz magnetic field has no effect on spatial learning in adult mice. *Bioelectromagnetics,* **17**(3), 249–52.

Sienkiewicz Z J, Haylock R G and Saunders R D (1996b). Acute exposure to power-frequency magnetic fields has no effect on the acquisition of a spatial learning task by adult male mice. *Bioelectromagnetics,* **17**(3), 180–86.

Sienkiewicz Z J, Haylock R G, Bartrum R, Saunders RD (1998a). 50 Hz magnetic field effects on the performance of a spatial learning task by mice. *Bioelectromagnetics,* **19**(8), 486–93.

Sienkiewicz Z J, Haylock R G, Saunders R D (1998b). Deficits in spatial learning after exposure of mice to a 50 Hz magnetic field. *Bioelectromagnetics,* **19**(2), 79–84.

Sienkiewicz Z J, Blackwell R P, Haylock R G E, Saunders R D and Cobb B L (2000). Low-level exposure to pulsed 900 MHz microwave radiation does not cause deficits in the performance of a spatial memory task *Bioelectromagnetics,* **21**, 151–8.

Sienkiewicz Z J, Bartram R, Haylock R G and Saunders R D (2001). Single, brief exposure to a 50 Hz magnetic field does not affect the performance of an object recognition task in adult mice. *Bioelectromagnetics,* **22**(1), 19–26.

Sikov M R, Mahlum D D, Montgomery L D and Decker J R (1979). Development of mice after intrauterine exposure to direct-current magnetic fields. IN *Biological Effects of Extremely Low Frequency Electromagnetic Fields* (R D Phillips, M F Gillis, W T Kaune and D D Mahlum, eds). 18th Hanford Life Sciences Symposium, Richland, Washington, October, 1978. Springfield VA, US Department of Energy, National Technical Information Service, p 462.

Silny J (1981). Influence of low-frequency magnetic field on the organism. IN Proceedings 4th Symposium on Electromagnetic Compatibility, Zurich, March 1981, pp 175–80.

Silny J (1984). Changes in VEP caused by strong magnetic fields. IN *Evoked Potentials II* (R H Nodar and C Barber, eds). Boston, Butterworth Publishers, pp 272–9.

Silny J (1985). Effects of low-frequency, high intensity magnetic field on the organism. IN Proceedings IEE International Conference on Electric and Magnetic Fields in Medicine and Biology, London, December 1985. London, IEE, pp 103–7.

Silny J (1986). The influence threshold of the time-varying magnetic field in the human organism. IN *Biological Effects of Static and Extremely Low Frequency Magnetic Fields* (J H Bernhardt, ed). München MMV, Medizin Verlag, pp 105–12.

Silny J (1999). Electrical hypersensitivity in humans – fact or fiction? *Zentralbl Hyg Umweltmed,* **202**(2–4), 219–33.

Simko M, Kriehuber R, Weiss D G and Luben R A (1998). Effects of 50 Hz EMF exposure on micronucleus formation and apoptosis in transformed and nontransformed human cell lines. *Bioelectromagnetics,* **19**(2), 85–91.

Skauli K S, Reitan J B and Walther B T (2000). Hatching in zebrafish *(Danio rerio)* embryos exposed to a 50 Hz magnetic field. *Bioelectromagnetics,* **21**(5), 407–10.

Skinner J, Mee T J, Blackwell R P, et al (2002). Exposure to power frequency electric fields and the risk of childhood cancer in the UK. *Br J Cancer,* **87**, 1257–66.

Smith R F, Clarke R L and Justesen D R (1994). Behavioral sensitivity of rats to extremely-low-frequency magnetic fields. *Bioelectromagnetics,* **15**(5), 411–26.

Smythe J W and Costall B (2003). Mobile phone use facilitates memory in male, but not female, subjects. *Neuroreport,* **14**(2), 243–6.

Sonnier H, Kolomytkin O V and Marino A A (2000). Resting potential of excitable neuroblastoma cells in weak magnetic fields. *Cell Mol Life Sci,* **57**(3), 514–20.

Sorahan T and Gilthorpe M S (1994). Non-differential misclassification of exposure always leads to an underestimate of risk: an incorrect conclusion. *Occup Environ Med,* **51**, 839–40.

Sorahan T, Nichols L, van Tongeren M and Harrington J M (2001). Occupational exposure to magnetic fields relative to mortality from brain tumours: updated and revised findings from a study of United Kingdom electricity generation and transmission workers. *Occup Environ Med,* **58**, 626–30.

SPTEC (2000). Scottish Parliament Transport and the Environment Committee Third Report. Report on inquiry into the proposals to introduce new planning procedures for telecommunications developments. http://www.scottish.parliament.uk/S1/official_report/cttee/trans-00/trr00-03-01.htm.

Stagg R B, Hawel L H III, Pastorian K, Cain C, Adey W R and Byus C V (2001). Effect of immobilization and concurrent cxposure to a pulse-modulated microwave field on core body temperature, plasma ACTH and corticosteroid, and brain ornithine decarboxylase, Fos and Jun mRNA. *Radiat Res,* **155**, 584–92.

Stagg R B, Thomas W J, Jones R A and Adey W R (1997). DNA synthesis and cell proliferation in C6 glioma and primary glial cells exposed to a 836.55 MHz modulated radiofrequency field. *Bioelectromagnetics,* **18**, 230–36.

Stang A, Anastassiou G, Ahrens W, Bromen K, Bornfeld N and Jockel K H (2001). The possible role of radiofrequency radiation in the development of uveal melanoma. *Epidemiology,* **12**, 7–12.

Stärk K D C, Krebs T, Altpeter E, Manz B, Griot C and Abelin T (1997). Absence of chronic effect of exposure to short-wave radio broadcast signal on salivary melatonin concentrations in dairy cattle. *J Pineal Res,* **22**, 171–6.

Stell M, Sheppard A R and Adey W R (1993). The effect of moving air on detection of a 60 Hz electric field. *Bioelectromagnetics,* **14**(1), 67–78.

Sterling P (1998). Retina. IN *The Synaptic Organisation of the Brain* (G M Shepherd, ed). New York, Oxford University Press, 205–54.

Stern S and Justesen D R (1995). Comments on 'Do rats show a behavioural sensitivity to low-level magnetic fields?' (letter and reply). *Bioelectromagnetics,* **16**, 335–8.

Stern S, Laties V G, Nguyen Q A and Cox C (1996). Exposure to combined static and 60 Hz magnetic fields: failure to replicate a reported behavioral effect. *Bioelectromagnetics,* **17**(4), 279–92.

Stern R M (1987). Cancer incidence among welders: possible effects of exposure to extremely low frequency electromagnetic radiation (ELF) and to welding fumes. *Environ Health Perspect,* **76**, 221–9.

Stevens P (2001). Effects of 5 s exposures to a 50 μT, 20 Hz magnetic field on skin conductance and ratings of affect and arousal. *Bioelectromagnetics,* **22**(4), 219–23.

Stevens R G (1987). Electric power use and breast cancer: a hypothesis. *Am J Epidemiol,* **125**(4), 556–61.

Stevens R G (1994). Re: 'Magnetic fields and cancer in children residing near Swedish high-voltage power lines'. *Am J Epidemiol,* **140**(1), 75.

Stevens R G, Wilson B W and Anderson L E (1997). *The Melatonin Hypothesis: Breast Cancer and Use of Electric Power.* Columbus, Battelle Press.

Stollery B T (1985). Human exposure to 50 Hz electric currents. IN *Biological Effects and Dosimetry of Static and ELF Electromagnetic Fields* (M Grandolfo, S M Michaelson A Rindi, eds). New York, Plenum Press, pp 445–54.

Stollery B T (1986). Effects of 50 Hz electric currents on mood and verbal reasoning skills. *Br J Ind Med,* **43**(5), 339–49.

Stollery B T (1987). Effects of 50 Hz electric currents on vigilance and concentration. *Br J Ind Med,* **44**(2), 111–18.

Stolwijk J A J (1970). A mathematical model of physiological temperature regulation in man. NASA-9-9531.

Stuchly M A and Dawson T W (2000). Interaction of low-frequency electric and magnetic fields with the human body. *Proc IEEE,* **88**(5), 643–64.

Stuchly M A and Gandhi O P (2000). Inter-laboratory comparison of numerical dosimetry for human exposure to 60 Hz electric and magnetic fields. *Bioelectromagnetics,* **21**, 167–74.

Stuchly M A, McLean J R, Burnett R, Goddard M, Lecuyer D W and Mitchel R E (1992). Modification of tumor promotion in the mouse skin by exposure to an alternating magnetic field. *Cancer Lett,* **65**(1), 1–7.

SSI (2003). Recent research on mobile telephony and cancer and other selected biological effects: first annual report from SSI's Independent Expert Group on Electromagnetic Fields. http://www.ssi.se/english/ EMF_exp_Eng_2003.pdf

STUK (1999). Radiation safety of handheld mobile phones and base stations. (Jokela K, Leszczynski D, Paile W, Salomaa S, Puranen L and Hyysalo P.) Helsinki, Finland, Radiation and Nuclear Safety Authority, Publication Number A161.

Suda T and Ueno S (1999). Control of the orientation of human erthrocytes by magnetic and electric fields. *J Appl Phys,* **85**(8), 5711–13.

Sukkar M Y, El-Munshid H A and Ardawi M S M, eds (2000). *Concise Human Physiology.* Oxford, Blackwell Science Ltd.

Suri A, deBoer J, Kusser W and Glickman B W (1996). A 3 milliTesla 60 Hz magnetic field is neither mutagenic nor co-mutagenic in the presence of menadione and MNU in a transgenic rat cell line. *Mutat Res,* **372**(1), 23–31.

Suzuki Y, Ikehata M, Nakamura K, Nishioka M, Asanuma K, Koana T and Shimizu H (2001). Induction of micronuclei in mice exposed to static magnetic fields. *Mutagenesis,* **16**(6), 499–501.

Svedenstal B M, Johanson K J and Mild K H (1999a). DNA damage induced in brain cells of CBA mice exposed to magnetic fields. *In Vivo,* **13**, 551–2.

Svedenstal B M, Johanson K J, Mattsson M O and Paulsson L E (1999b). DNA damage, cell kinetics and ODC activities studied in CBA mice exposed to electromagnetic fields generated by transmission lines. *In Vivo,* **13**, 507–13.

Sweetland J, Kertesatz A, Prato F S and Nantau K (1987). The effect of magnetic resonance imaging on human cognition. *Magn Reson Imaging,* **5**, 129–35.

Swerdlow A J (1999). Measurement of radiofrequency radiation exposure in epidemiological studies. *Radiat Prot Dosim,* **83**, 149–53.

Swerdlow A J (2003). Shift work and breast cancer: a critical review of the epidemiological evidence. Prepared by the Institute of Cancer Research for the Health and Safety Executive. Sudbury, HSE, Research Report 132.

Sykes P J, McCallum B D, Bangay M J, Hooker A M and Morley AA (2001). Effect of exposure to 900 MHz radiofrequency radiation on intrachromosomal recombination in pKZ1 mice. *Radiat Res,* **156**(5 Part 1), 495–502.

Tablado L, Perez-Sanchez F and Soler C (1996). Is sperm motility maturation affected by static magnetic fields? *Environ Health Perspect,* **104**(11), 1212–16.

Tablado L, Perez-Sanchez F, Nunez J, Nunez M and Soler C (1998). Effects of exposure to static magnetic fields on the morphology and morphometry of mouse epididymal sperm. *Bioelectromagnetics,* **19**(6), 377–83.

Tablado L, Soler C, Nunez M, Nunez J and Perez-Sanchez F (2000). Development of mouse testis and epididymis following intrauterine exposure to a static magnetic field. *Bioelectromagnetics,* **21**(1), 19–24.

Tabrah F L, Mower H F, Batkin S and Greenwood P B (1994). Enhanced mutagenic effect of a 60 Hz time-varying magnetic field on numbers of azide-induced TA100 revertant colonies. *Bioelectromagnetics,* **15**(1), 85–93.

Taflove A (1995). *Computational Electromagnetics – the Finite-Difference Time-Domain Method.* London, Artech.

Takahashi S, Inaguma S, Cho Y M, Imaida K, Wang J, Fujiwara O and Shirai T (2002). Lack of mutation induction with exposure to 1.5 GHz electromagnetic near fields used for cellular phones in brains of Big Blue mice. *Cancer Res,* **62**(7), 1956–60.

Taki M, Suzuki Y and Wake K (2003). Dosimetry considerations in the head and retina for extremely low frequency electric fields. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 349–56.

Taoka S, Padmakumar R, Grissom C B and Banerjee R (1997). Magnetic field effects on coenzyme B12-dependent enzymes: validation of ethanolamine ammonia lyase results and extension to human methylmalonyl CoA mutase. *Bioelectromagnetics,* **18**(7), 506–13.

Tattersall J E, Scott I R, Wood S J, Nettell J J, Bevir M K, Wang Z, Somasiri NP and Chen X (2001). Effects of low intensity radiofrequency electromagnetic fields on electrical activity in rat hippocampal slices. *Brain Res,* **904**(1), 43–53.

Tenforde T S (1992). Interaction mechanisms and biological effects of static magnetic fields. *Automedica,* **14**, 271–93.

Tenforde T S and Shrifrine M (1984). Assessment of the immune responsiveness of mice exposed to a 1.5-tesla stationary magnetic field. *Bioelectromagnetics,* **5**, 443.

Tenforde T S, Gaffey C T, Moyer B R and Budinger T F (1983). Cardiovascular alterations in Macaca monkeys exposed to stationary magnetic fields: experimental observations and theoretical analysis. *Bioelectromagnetics,* **4**, 1.

Tenforde T S, Gaffey C T, Liburdy R P and Levy L (1985). Biological effects of magnetic fields. IN Biology and Medicine Division Annual Report 1985, Lawrence Berkeley Laboratories, LBL 20345. Berkeley, University of California, p 60.

Tenforde T S, Levy L and Veklerov E (1987). Monitoring of circadian waveforms in rodents exposed to high-intensity magnetic fields. IN *Interaction of Biological Systems with Static and ELF Electric and Magnetic Fields* (L E Anderson, B J Kelman and R J Weigel, eds). 23rd Hanford Life Sciences Symposium, Richland, Washington, October 1984. Richland, Pacific Northwest Laboratory, p 307.

Terol F F and Panchon A (1995). Exposure of domestic quail embryos to extremely low frequency magnetic fields. *Int J Radiat Biol,* **68**(3), 321–30.

Testylier G, Tonduli L, Malabiau R and Debouzy J C (2002). Effects of exposure to low level radiofrequency fields on acetylcholine release in hippocampus of freely moving rats. *Bioelectromagnetics,* **23**(4), 249–55.

Thach J S Jr (1968). A behavioral effect of intense D-C electromagnetic fields. IN *Use of Non-human Primates in Drug Evaluation* (H Vagtborg, ed). Austin, Texas, University of Texas Press, p 347.

Thériault G, Goldberg M, Miller A B, Armstrong B, Guenel P, Deadman J, Imbernon E, To T, Chevalier A, Cyr D, et al (1994). Cancer risks associated with occupational exposure to magnetic fields among electric utility workers in Ontario and Quebec, Canada, and France: 1970–1989. *Am J Epidemiol,* **139**, 550–72.

Thomas A W and Persinger M A (1997). Daily post-training exposure to pulsed magnetic fields that evoke morphine-like analgesia affects consequent motivation but not proficiency in maze learning in rats. *Electro- Magnetobiol,* **16**, 33–41.

Thomas J R, Schrot J and Liboff A R (1986). Low-intensity magnetic fields alter operant behavior in rats. *Bioelectromagnetics,* **7**(4), 349–57.

Thun-Battersby S, Mevissen M and Löscher W (1999). Exposure of Sprague-Dawley rats to a 50-hertz, 100-μtesla magnetic field for 27 weeks facilitates mammary tumorigenesis in the 7,12-dimethylbenz[a]-anthracene model of breast cancer. *Cancer Res,* **59**(15), 3627–33.

Thuroczy G, Kubinyi G, Sinay H, Bakos J, Sipos K, Lenart A and Szabo L D (1994). Simultaneous response of brain electrical activity (EEG) and cerebral circulation (REG) to microwave exposure in rats. *Rev Environ Health,* **10**, 135–48.

Tian F, Nakahara T, Wake K, Taki M and Miyakoshi J (2002). Exposure to 2.45 GHz electromagnetic fields induces hsp70 at a high SAR of more than 20 W/kg but not at 5 W/kg in human glioma MO54 cells. *Int J Radiat Biol,* **78**(5), 433–40.

Tice R R, Hook G G, Donner M, McRee D I and Guy A W (2002). DNA damage and micronuclei induction in cultured human blood cells. *Bioelectromagnetics,* **23**, 113–26.

Tinniswood A D, Furse C M and Gandhi O P (1998). Power deposition in the head and neck of an anatomically based human body model for plane wave exposure. *Phys Med Biol,* **43**, 2361–78.

Toler J C, Shelton W W, Frei M R, Merritt J H and Stedham M A (1997). Long-term, low-level exposure of mice prone to mammary tumors to 435 MHz radiofrequency radiation. *Radiat Res,* **148**, 227–34.

Tremblay L, Houde M, Mercier G, Gagnon J and Mandeville R (1996). Differential modulation of natural and adaptive immunity in Fischer rats exposed for 6 weeks to 60 Hz linear sinusoidal continuous-wave magnetic fields. *Bioelectromagnetics,* **17**(5), 373–83.

Trimmel M and Schweiger E (1998). Effects of an ELF (50 Hz, 1 mT) electromagnetic field (EMF) on concentration in visual attention, perception and memory including effects of EMF sensitivity. *Toxicol Lett,* **96–97**, 377–82.

Truong H and Yellon SM (1997). Effect of various acute 60 Hz magnetic field exposures on the nocturnal melatonin rise in the adult Djungarian hamster. *J Pineal Res,* **22**(4), 177–83.

Truong H, Smith J C and Yellon S M (1996). Photoperiod control of the melatonin rhythm and reproductive maturation in the juvenile djungarian hamster: 60 Hz magnetic field exposure effects. *Biol Reprod,* **55**, 455–60.

Trzeciak H I, Grzesik J, Bortel M, Kuska R, Duda D, Michnik J and Malecki A (1993). Behavioral effects of long-term exposure to magnetic fields in rats. *Bioelectromagnetics,* **14**(4), 287–97.

Tsuji Y, Nakagawa M and Suzuki Y (1996). Five-tesla static magnetic fields suppress food and water consumption and weight gain in mice. *Ind Health,* **34**(4), 347–57.

Tsurita G, Nagawa H, Ueno S, Watanabe S and Taki (2000). Biological and morphological effects on the brain after exposure of rats to a 1439 MHz TDMA field. *Bioelectromagnetics,* **21**, 364–71.

Tuinstra R, Goodman E and Greenebaum B (1998). Protein kinase C activity following exposure to magnetic field and phorbol ester. *Bioelectromagnetics,* **19**(8), 469–76.

Tyndall D A (1993). MRI effects on craniofacial size and crown-rump length in C57BL/6J mice in 1.5 T fields. *Oral Surg Oral Med Oral Pathol,* **76**(5), 655–60.

Tyndall D A (1990). MRI effects on the teratogenicity of x-irradiation in the C57BL/6J mouse. *Magn Reson Imaging,* **8**(4), 423–33.

Tynes T, Klaeboe L and Haldorsen T (2003). Residential and occupational exposure to 50 Hz magnetic fields and malignant melanoma: a population based study. *Occup Environ Med,* **60**, 343–7.

Uckun F M, Kurosaki T, Jin J, Jun X, Morgan A, Takata M, Bolen J and Luben R (1995). Exposure of B-lineage lymphoid cells to low energy electromagnetic fields stimulates Lyn kinase. *J Biol Chem,* **270**(46), 27666–70.

Ueno S (1999). Biomagnetic approaches to studying the brain. *IEEE Eng Med Biol Magn,* **18**, 108–20.

Ueno S and Iwasaka M (1994a). Properties of diamagnetic fluid gradient magnetic fields. *J Appl Phys,* **75**(10), 7177–9.

Ueno S and Iwasaka M (1994b). Parting of water by magnetic fields. *IEEE Trans Magn,* **30**(6), 4698–700.

Ueno S and Iwasaka M (1999). Effects and mechanisms of intense DC magnetic fields on biological, physical, and chemical processes. IN *Electricity and Magnetism in Biology and Medicine* (F Bersani, ed). New York, Kluwer Academic/Plenum, pp 205–10.

Ueno S, Iwasaka M and Shiokawa K (1994a). Early embryonic development of frogs under intense magnetic fields up to 8 T. *J Appl Phys,* **75**(10), 7165–67.

Ueno S, Iwasaka M and Kitajima T (1994b). Redistribution of dissolved oxygen concentration under magnetic fields up to 8 T. *J Appl Phys,* **75**(10), 7174–6.

UK Childhood Cancer Study Investigators (1999). Exposure to power frequency magnetic fields and the risk of childhood cancer. *Lancet,* **354**, 1925–31.

UN (1982). United Nations General Assembly – 48th Plenary Meeting. World Charter for Nature. http://www.un.org/documents/ga/res/37/a37r007.htm.

UNSCEAR (1986). United Nations Scientific Committee on the Effects of Atomic Radiation. Biological effects of pre-natal irradiation. Annex C. IN Genetic and Somatic Effects of Ionising Radiation. Report to the General Assembly with scientific annexes. New York, United Nations, pp 263–6.

UNSCEAR (2000). United Nations Scientific Committee on the Effects of Atomic Radiation. Report to the General Assembly with scientific annexes. New York, United Nations.

Utteridge T D, Gebski V, Finnie J W, Vernon-Roberts B and Kuchel T R (2002). Long-term exposure of Eμ-Pim1 transgenic mice to 898.4 MHz microwaves does not increase lymphoma icidence. *Radiat Res,* **158**(3), 357–64.

Utteridge T D, Gebski V, Finnie J W, Vernon-Roberts B and Kuchel T R (2003). Response to the letters to the Editor sent by (1) Kundi, (2) Goldstein/Kheiferts/van Deventer/Repacholi, and (3) Lerchl. *Radiat Res,* **159**, 276–8.

Vähä-Eskeli K, Erkkola R and Seppänen A (1991). Is the heat-dissipating ability enhanced during pregnancy? *Eur J Obstet Gynecol Reprod Biol,* **39**, 169–74.

Valberg P A, Kavet R and Rafferty C N (1997). Can low level 50/60 Hz electric and magnetic fields cause biological effects? *Radiat Res,* **148**(1), 2–21.

van Leeuwen G M, Lagendijk J J, Van Leersum B J, Zwamborn A P, Hornsleth S N and Kotte A N (1999). Calculation of change in brain temperatures due to exposure to a mobile phone. *Phys Med Biol,* **44**(10), 2367–79.

van Wijngaarden E (2003). An exploratory investigation of suicide and occupational exposure. *J Occup Environ Med,* **45**, 96–101.

van Wijngaarden E, Savitz D A, Kleckner R C, Cai J and Loomis D (2000). Exposure to electromagnetic fields and suicide among electric utility workers: a nested case–control study. *West J Med,* **173**, 94–100.

Verschaeve L and Maes A (1998). Genetic, carcinogenic and teratogenic effects of radiofrequency fields. *Mutat Res,* **410**, 141–65.

Veyret B (2003). Rapporteur report: interaction mechanisms. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 317–20.

Veyret B, Hansson Mild K, Miro L, Simunic D, et al (1999). Possible Health Effects Related to the Use of Radiotelephones. European Commission Expert Group Report. Brussels, European Commission.

Vijayalaxmi, Frei M R, Dusch S J, Guel V, Meltz M L and Jauchem J R (1997a). Frequency of micronuclei in the peripheral blood and bone marrow of cancer-prone mice chronically exposed to 2450 MHz radiofrequency radiation. *Radiat Res,* **147**, 495–500.

Vijayalaxmi, Frei M, Dusch S J, Guel V, Meltz M and Jauchem J R (1997b). Correction of an error in calculation in the article 'Frequency of micronuclei in the peripheral blood and bone marrow of cancer-prone mice chronically exposed to 2450 MHz radiofrequency radiation' (*Radiat Res,* **147**, 495–500). *Radiat Res,* **149**, 308–12.

Vijayalaxmi, Mohan N, Meltz M L, Wittler M A (1997c). Proliferation and cytogenetic studies in human blood lymphocytes exposed *in vitro* to 2450 MHz radiofrequency radiation. *Int J Radiat Biol,* **72**, 751–7.

Vijayalaxmi, Seaman R L, Belt M L, Doyle J M, Mathur S P and Prihoda T J (1999). Frequency of micronuclei in the blood and bone marrow cells of mice exposed to ultra-wideband electromagnetic radiation. *Int J Radiat Biol,* **75**, 115–20.

Vijayalaxmi, Leal B Z, Szilagyi M, Prihoda T J and Meltz M L (2000). Primary DNA damage in human blood lymphocytes exposed *in vitro* to 2450 MHz radiofrequency radiation. *Radiat Res,* **153**(4),479–86.

Vijayalaxmi, Pickard W F, Bisht K S, Prihoda T J, Meltz M L, LaRegina M C, Roti Roti J L, Straube W L and Moros E G (2001a). Micronuclei in the peripheral blood and bone marrow cells of rats exposed to 2450 MHz radiofrequency radiation. *Int J Radiat Biol,* **77**, 1109–15.

Vijayalaxmi, Bisht K S, Pickard W F, Meltz M L, Roti Roti J L and Moros E G (2001b). Chromosome damage and micronucleus formation in human blood lymphocytes exposed *in vitro* to radiofrequency radiation at a cellular telephone frequency (847.74 MHz, CDMA). *Radiat Res,* **156**, 430–32.

Vijayalaxmi, Leal B Z, Meltz M L, Pickard W F, Bisht K S, Roti Roti J L, Straube W L and Moros E G (2001c). Cytogenetic studies in human blood lymphocytes exposed *in vitro* to radiofrequency radiation at a cellular telephone frequency (835.62 MHz, FDMA). *Radiat Res,* **155**, 113–21.

Villeneuve P J, Agnew D A, Johnson K C and Mao Y (2002). Brain cancer and occupational exposure to magnetic fields among men: results from a Canadian population-based case–control study. *Int J Epidemiol,* **31,** 210–17.

Vollrath L, Spessert R, Kratzsch T, Keiner M and Hollman H (1997). No short-term effects of high-frequency electromagnetic fields on the mammalian pineal gland. *Bioelectromagnetics,* **18**, 376–87.

Vorobyov V V, Galchenko A A, Kukushkin N L and Akoev I G (1997). Effects of weak microwave fields amplitude modulated at ELF on EEG of symmetric brain areas in rats. *Bioelectromagnetics,* **18**, 293–8.

Wachtel H (1992). Bioelectric background fields and their implications for ELF dosimetry. *Bioelectromagnetics,* **Suppl 1**, 139–45.

Wagner P, Roschke J, Mann K, Hiller W and Frank C (1998). Human sleep under the influence of pulsed radiofrequency electromagnetic fields: a polysomnographic study using standardized conditions. *Bioelectromagnetics,* **19**(3), 199–202.

Wagner P, Roschke J, Mann K, Fell J, Hiller W, Frank C and Grozinger M (2000). Human sleep EEG under the influence of pulsed radio frequency electromagnetic fields. Results from polysomnographies using submaximal high power flux densities. *Neuropsychobiology,* **42**(4), 207–12.

Wainwright P R (2000). Thermal effects of radiation from cellular telephones. *Phys Med Biol,* **45**, 2363–72.

Wake K, Tanaka T, Kawasumi M and Taki M (1998). Induced current density distribution in a human related to magnetophosphenes. *Trans IEE Jpn,* **118-A**, 806–11.

Walleczek J (1995). Magnetokinetic effects on radical pairs: a paradigm for magnetic field interactions with biological systems at lower than thermal energy. IN *Electromagnetic fields: Biological Interactions and Mechanisms* (Advances in Chemistry 250) (M Blank, ed). Washington DC, American Chemical Society, pp 395–420.

Walleczek J, Killoran P L and Adey W R (1994). 60 Hz magnetic field effects on Ca^{2+} (Mn^{2+}) influx in human Jurkat T-cells: strict dependency on cell state. IN Abstracts, 16th Annual Meeting of the Bioelectromagnetics Society, Copenhagen, June 1994, p 76.

Walleczek J, Shiu E C and Hahn G M (1999). Increase in radiation-induced HPRT gene mutation frequency after nonthermal exposure to nonionizing 60 Hz electromagnetic fields. *Radiat Res,* **151**(4), 489–97.

Walsh V and Cowey A (1998). Magnetic stimulation studies of visual cognition. *Trends Cogn Sci,* **2**(3), 103–10.

Walters T J, Mason P A, Sherry C J, Steffen C and Merritt J H (1995). No detectable bioeffects following acute exposure to high peak power ultra-wide band electromagnetic radiation in rats. *Aviat, Space Environ Med,* **66**, 562–7.

Walters T J, Blick D W, Johnson L R, Adair E R and Foster K R (2000). Heating and pain sensation produced in human skin by millimeter waves: comparison to a simple thermal model. *Health Phys,* **78**, 259–67.

Wang B and Lai H (2000). Acute exposure to pulsed 2450-MHz microwaves affects water-maze performance of rats. *Bioelectromagnetics,* **21**(1), 52–6.

Wang J and Fujiwara O (1999). FDTD computation of temperature rise in the human head for portable telephones. *IEEE Trans Microwave Theory Techniq,* **47**, 1528–34.

Wang Y-P, Yuan S-L, Chen X-H, Yang Y, Song Y and Chen N-Y (2001). Experimental study of apoptosis and its molecular mechanisms of nasopharyngeal carcinoma cell induced by millimeter wave irradiation. *Journal of Infrared and Millimeter Waves,* **20**, 283–6.

Warman G R, Tripp H M, Warman V L and Arendt J (2003). Circadian neuro-endocrine physiology and electromagnetic field studies: precautions and complexities. IN Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4), 369–74.

Warren H G, Prevatt A A, Daly K A and Antonelli P J (2003). Cellular telephone use and risk of intratemporal facial nerve tumor. *Laryngoscope,* **113**, 663–7.

Wartenberg M, Hescheler J and Sauer H (1997). Electrical fields enhance growth of cancer spheriods by reactive oxygen species and intra cellular Ca^{2+}. *Am J Physiol,* **272**(5 Part 2), R1677–83.

Wasserman E M (1998). Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation, June 1996. *Electroenceph Clin Neurophys,* **108**, 1–16.

Watanabe A (1959). The effect of heat on the human spermatogenesis. *Kyushu J Med Sci,* **10**, 101–17.

Watanabe S, Taki M, Nojima T and Fujiwara (1996). Characteristics of the SAR distributions in a head exposed to electromagnetic fields radiated by a hand-held portable radio. *IEEE Trans Microwave Theory Techniq,* **44**, 1874–83.

Watanabe Y, Nakagawa M and Miyakoshi Y (1997). Enhancement of lipid peroxidation in the liver of mice exposed to magnetic fields. *Ind Health,* **35**(2), 285–90.

Watanabe Y, Tanaka T, Taki M and Watanabe S-i (2000). FDTD analysis of microwave hearing effect. *IEEE Trans Microwave Theory Techniq,* **48**, 2126–32.

Weast R C (ed) (1980). *CRC Handbook of Chemistry and Physics* (61st Edition). Boca Raton, CRC Press.

Weigel R J, Jaffe R A, Lundstrom D L, Forsythe W C and Anderson L E (1987). Stimulation of cutaneous mechanoreceptors by 60 Hz electric fields. *Bioelectromagnetics,* **8**(4), 337–50.

Weiland T (1990). Maxwell's grid equations. *Frequenz,* **44**, 9–16.

Weinbaum S and Jiji L M (1985). A new simplified bioheat equation for the effect of blood flow on local average tissue temperature. *ASME J Biomech Eng,* **107**, 131–9.

Weiss J, Herrick R C, Taber K H, Contant C and Plishker G A (1992). Bio-effects of high magnetic fields: a study using a simple animal model. *Magn Reson Imaging,* **10**(4), 689–94.

Wey H E, Conover D P, Mathias P, Toraason M and Lotz W G (2000). 50-hertz magnetic field and calcium transients in Jurkat cells: results of a research and public information dissemination (RAPID) program study. *Environ Health Perspect,* **108**(2), 135–40.

Whittington C J, Podd J V and Rapley B R (1996). Acute effects of 50 Hz magnetic field exposure on human visual task and cardiovascular performance. *Bioelectromagnetics,* **17**(2), 131–7.

WHO (1946). World Health Organization. Preamble to the Constitution of WHO as adopted by the International Health Conference, New York, June 1946. Official Records of the World Health Organization, No. 2, 100. http://whqlibdoc.who.int/hist/official_records/constitution.pdf.

WHO (1987). Magnetic Fields. Geneva, World Health Organization, Environmental Health Criteria 69.

WHO (1993). Electromagnetic Fields (300 Hz – 300 GHz). Geneva, World Health Organization, Environmental Health Criteria 137.

WHO (2000). Electromagnetic Fields and Public Health – Cautionary Policies. WHO Backgrounder. March 2000. http://www.who.int/docstore/peh-emf/publications/facts_press/EMF-Precaution.htm.

WHO (2003a). WHO Precautionary Framework for Public Health Protection (Draft for Review – 11 July 2003). Geneva, World Health Organization.

WHO (2003b). Adverse Temperature Levels in the Human Body. Proceedings of a Workshop. Geneva, March 2002. *Int J Hyperthermia,* **19**(3).

Wieraszko A (2000). Dantrolene modulates the influence of steady magnetic fields on hippocampal evoked potentials *in vitro*. *Bioelectromagnetics,* **21**(3), 175–82.

Willett E V, McKinney P A, Fear N T, Cartwright R A and Roman E (2003). Occupational exposure to electromagnetic fields and acute leukaemia: analysis of a case–control study. *Occup Environ Med,* **60**, 577–83.

Wilson B W, Anderson L E, Hilton D I and Phillips R D (1981). Chronic exposure to 60 Hz electric fields: effects on pineal function in the rat. *Bioelectromagnetics,* **2**(4), 371–80.

Wilson B W, Anderson L E, Hilton D I and Phillips R D (1983). Erratum. Chronic exposure to 60 Hz electric fields: effects on pineal function in the rat [1981, **2**, 371–80]. *Bioelectromagnetics,* **4**, 293.

Wilson B W, Chess E K and Anderson L E (1986). 60 Hz electric-field effects on pineal melatonin rhythms: time course for onset and recovery. *Bioelectromagnetics,* **7**(2), 239–42.

Wilson B W, Wright C W, Morris J E, Buschborn R L, Brown D P, Miller D L, Sommers-Flannigan R and Anderson L E (1990). Evidence for an effect of ELF electromagnetic fields on human pineal gland function. *J Pineal Res,* **9**(4), 259–69.

Wilson B W, Matt K S, Morris J E, Sasser L B, Miller D L and Anderson L E (1999). Effects of 60 Hz magnetic field exposure on the pineal and hypothalamic-pituitary-gonadal axis in the Siberian hamster *(Phodopus sungorus). Bioelectromagnetics,* **20**(4), 224–32.

Winther F O, Rasmussen K, Tvete O, Halvorsen U and Haugsdal B (1999). Static magnetic field and the inner ear. A functional study of hearing and vestibular function in man after exposure to a static magnetic field. *Scand Audiol,* **28**(1), 57–9.

Wiskirchen J, Groenewaeller E F, Kehlbach R, Heinzelmann F, Wittau M, Rodemann H P, Claussen C D and Duda S H (1999). Long-term effects of repetitive exposure to a static magnetic field (1.5 T) on proliferation of human fetal lung fibroblasts. *Magn Reson Med,* **41**(3), 464–8.

Wiskirchen J, Gronewaller E F, Heinzelmann F, Kehlbach R, Rodegerdts E, Wittau M, Rodemann H P, Claussen C D and Duda S H (2000). Human fetal lung fibroblasts: *in vitro* study of repetitive magnetic field exposure at 0.2, 1.0, and 1.5 T. *Radiology,* **215**(3), 858–62.

Wolff S, Crooks L E, Brown P, Howard R and Painter R B (1980). Tests for DNA and chromosomal damage by nuclear magnetic resonance imaging. *Body Comput Tomog NMR,* **136**, 707.

Wood A W, Armstrong S M, Sait M L, Devine L and Martin M J (1998). Changes in human plasma melatonin profiles in response to 50 Hz magnetic field exposure. *J Pineal Res,* **25**(2), 116–27.

Wu R Y, Chiang H, Shao B J, Li N G and Fu Y D (1994). Effects of 2.45 GHz microwave radiation and phorbol ester 12-O-tetradecanoylphorbol-13-acetate on dimethylhydrazine-induced colon cancer in mice. *Bioelectromagnetics,* **15**, 531–8.

Xi W, Stuchly M A and Gandhi O P (1994). Induced electric currents in models of man and rodents from 60 Hz magnetic fields. *IEEE Trans Biomed Eng,* **41**, 1018–23.

Xu S, Okano H and Ohkubo C (1998). Subchronic effects of static magnetic fields on cutaneous microcirculation in rabbits. *In Vivo,* **12**(4), 383–9.

Yaguchi H, Yoshida M, Ejima Y and Miyakoshi J (1999). Effect of high-density extremely low frequency magnetic field on sister chromatid exchanges in mouse m5S cells. *Mutat Res,* **440**(2),189–94.

Yano M, Wang J and Fujiwara O (2001). FDTD computation of temperature rise in realistic head models simulating adult and infant for 1.5 GHz microwave exposure. *Electronics and Communications in Japan,* Part 1, **84**(4), 57–66.

Yasui M, Kikuchi T, Ogawa M, Otaka Y, Tsuchitani M and Iwata H (1997). Carcinogenicity test of 50 Hz sinusoidal magnetic fields in rats. *Bioelectromagnetics,* **18**(8), 531–40.

Yellon S M (1994). Acute 60 Hz magnetic field exposure effects on the melatonin rhythm in the pineal gland and circulation of the adult Djungarian hamster. *J Pineal Res,* **16**(3), 136–44.

Yellon S M (1996). 60-Hz magnetic field exposure effects on the melatonin rhythm and photoperiod control of reproduction. *Am J Physiol,* **270**(5 Part 1), E816–21.

Yellon S M and Truong H N (1998). Melatonin rhythm onset in the adult siberian hamster: influence of photoperiod but not 60-Hz magnetic field exposure on melatonin content in the pineal gland and in circulation. *J Biol Rhythms,* **13**(1), 52–9.

Yip Y P, Capriotti C, Talagala S L and Yip J W (1994a). Effects of MR exposure at 1.5 T on early embryonic development of the chick. *J Magn Reson Imaging,* **4**(5), 742–8.

Yip Y P, Capriotti C, Norbash S G, Talagala S L, Yip J W (1994b). Effects of MR exposure on cell proliferation and migration of chick motoneurons. *J Magn Reson Imaging,* **4**(6),799–804.

Yu M C, Gona A G, Gona O, al-Rabiai S, Von Hagen S and Cohen E (1993). Effects of 60 Hz electric and magnetic fields on maturation of the rat neopallium. *Bioelectromagnetics,* **14**(5), 449–58.

Zecca L, Mantegazza C, Margonato V, Cerretelli P, Caniatti M, Piva F, Dondi D, Hagino N (1998). Biological effects of prolonged exposure to ELF electromagnetic fields in rats: III. 50 Hz electromagnetic fields. *Bioelectromagnetics,* **19**(1), 57–66.

Zhadin M N, Deryugina O N and Pisachenko T M (1999). Influence of combined DC and AC magnetic fields on rat behavior. *Bioelectromagnetics,* **20**(6), 378–86.

Zmirou (2001). Mobile Phones, their Base Stations, and Health. Report to the French Health Directorate, Chairman, Denis Zmirou. France, Direction Générale de la Santé. http://www.sante.gouv.fr

Zook B C and Simmens S J (2001). The effects of 860 MHz radiofrequency radiation on the induction or promotion of brain tumors and other neoplasms in rats. *Radiat Res*, **155**, 572–83.

Zotti-Martelli L, Peccatori M, Scarpato R and, Migliore L (2000). Induction of micronuclei in human lymphocytes exposed *in vitro* to microwave radiation. *Mutat Res*, **472**, 51–8.

Zubal I G, Harrell C R, Smith E O, Rattner Z, Gindi G R and Hoffer P H (1994). Computerized three dimensional segmented human anatomy. *Phys Med Biol*, **21**, 299–302.

Zwamborn A P M, Vossen S H J A, van Leersum B J A M, Ouwens M A and Makel W N (2003). Effects of global communication system radio-frequency fields on well being and cognitive functions of human subjects with and without subjective complaints. Netherlands Organisation for Applied Scientific Research (TNO), FEL-03-C148.

Appendix A

WEAK ELECTRIC FIELDS GROUP

Position statement on weak electric field effects in humans and their implications for standards, following a meeting held at NRPB (22 November 2001), and subsequent discussion and correspondence

Members

Professor C Blakemore FRS (University of Oxford) (Chairman)
Professor D Attwell FRS (University College, London)
Professor J Jefferys (University of Birmingham)
Dr J Tattersall (Dstl, Porton Down and University of Southampton)
Dr R Saunders (NRPB, Chilton)
Dr Z Sienkiewicz (NRPB, Chilton)
Dr J Stather (NRPB, Chilton)

Purpose

The remit of the ad hoc expert group on effects of weak electric fields was to review the neurophysiological evidence for effects of induced electric fields and currents that could provide a basis for revised guidance on human exposure to time-varying electric and magnetic fields below 100 kHz.

Summary

The specific issues addressed included the suitability of the neuronal circuitry of the retina as a model for neuronal circuitry in the central nervous system (CNS), the evidence for weak electric field interactions in brain tissue *in vitro*, effects on coupled networks of neurons and extrapolation *in vivo*, effects on the developing nervous system, sensitive subgroups and the implications for standards. Many of these issues were raised in the discussion of the paper by Saunders and Jefferys (2002) and the earlier review by Jefferys (1995).

Suitability of the retina as a model for electric field interactions with the CNS

There was general agreement with the evidence and conclusions reached by Dr Saunders and Professor Jefferys in their joint paper cited above. In particular, the retina was considered to be a good, albeit especially sensitive, model for CNS neuronal circuitry*. Phosphenes can be reliably produced by electric fields induced in the retina or directly applied via electrodes; minimum threshold current densities (at 20 Hz) have been estimated by several authors (Adrian, 1977; Carstensen et al, 1985; Wake et al, 1998) as around 10–14 mA m^{-2}; if the conductance of retinal tissue is assumed to be similar to that of brain tissue, about 0.1 S m^{-1} (Gabriel, 1995), the equivalent threshold electric field value in the retina can be estimated as approximately 100–140 mV m^{-1}. These values are, however, subject to some uncertainty: the calculation by Wake et al

* Described, for example, by Shepherd (1998).

(1998) was based on high retinal conductivity of 1.5 S m^{-1} (Wake, personal communication, 2002). Adrian (1977) provided an order-of-magnitude threshold, based on a homogeneous head, and Carstensen et al (1985) used a 1600-element model of the head in which the retina was not accurately modelled, although the result was described as moderately robust to changes in model parameters.

Several lines of evidence suggested that the phototransduction apparatus was not involved in the induction of phosphenes by induced weak electric fields: Carpenter (1972) had shown that phosphene threshold did not show the dark adaptation behaviour characteristic of photoreceptors, and a study cited by Saunders and Jefferys indicated phosphenes could be induced in a blind patient suffering with a degenerative condition (retinitis pigmentosa) affecting the pigment epithelium and photoreceptor layer. Other properties favoured the retina as a sensitive indicator of weak electric field interactions with CNS neuronal circuits, namely: its peripheral location, its highly ordered structure, and the predominantly non-spiking (ie graded, electrotonic) behaviour of many of its neuronal elements, namely the horizontal, bipolar and (most) amacrine cells, as well as the photoreceptors. These various factors, and the tight electrical coupling that exists between some groups of retinal cells, were thought to render the retina relatively sensitive but not unrepresentative of the response of other CNS neuronal circuits to induced electric fields.

Highly ordered regions of the CNS such as the cerebral cortex, hippocampus and cerebellum, with tightly aligned dendritic fields and restricted extracellular space, would favour weak electric field interactions (Faber and Korn, 1989; Jefferys, 1995; Saunders and Jefferys, 2002) compared with more diffuse structures such as the thalamus or striatum. The group noted that the anisotropy exhibited by these tissues is likely to engender a degree of directional sensitivity to induced electric fields, which is unlikely to be accounted for in the measurement of the dielectric properties of these tissues.

Weak electric field effects on the adult CNS

The evidence concerning weak electric field effects in CNS (predominantly hippocampal) tissue *in vitro*, summarised by Jefferys (1995) and more briefly by Saunders and Jefferys (2002), was considered. Jefferys (1995) concluded that weak induced fields of the order of 4 V m^{-1} could affect excitability and synchronicity in neuronal tissue; however, it was noted at the meeting that this response appeared to vary linearly with the applied field. Subsequently, effects have been reported at induced electric fields as low as 400 mV m^{-1} (Francis et al, 2000). Recently, Gluckman, Schiff and colleagues (Gluckman et al, 2001) using an *in vitro* model of epilepsy, reported detection limits for modulation of single neurons and networks by electric fields near the 100 mV m^{-1} range. Consideration should also be given to the possible effects of electric fields on glia as well as on neurons since:

(a) on theoretical grounds, spatially extended cells may be more sensitive to external electric fields,
(b) glial cells form a large network interconnected by gap junctions,
(c) recent work has shown that $[Ca]_i$ elevations in glia can trigger release of the neurotransmitter glutamate from glia (Parpura et al, 1994; Hassinger et al, 1995; Bezzi et al, 1998, 2001).

The relevance of these *in vitro* data to possible effects on the CNS *in vivo* was discussed. In general, support was expressed for the view taken by Saunders and Jefferys (2002) that thresholds were likely to be lower, both as a result of the higher levels of spontaneous activity, and of the potential involvement of large, interacting groups of nerve cells (neural networks). In particular, much of normal brain function depends on the collective activity of very large numbers of neurons; network modelling is widely used in the investigation of neuronal behaviour in the central nervous system*. It was noted that the integration of a very weak effect on a large number of interacting nerve cells would result in an increase in signal-to-noise ratio proportional to the square root of the number of interacting cells, assuming independent noise. It is thought that the minimum number of cells involved, for example, in epileptic activity in the hippocampus is about 1000 (Jefferys, 1994) with a volume of approximately 0.5–1 mm^3.

The potential frequency response of these weak field effects was discussed. Attention was drawn to the view that the limited frequency response of phosphenes results from time constants for synaptic activity (around 20 ms) that are about 100 times longer than those associated with, for example, peripheral nerve activity (Reilly, 1999; IEEE, 2002). However, many kinds of neuronal dendrites do not necessarily satisfy passive cable theory (Tagaki, 2000). They contain voltage-gated ion channels capable of propagating transient potentials, which may additionally modulate dendritic function. The group expressed the opinion that effects at frequencies up to a few kilohertz should not be ruled out, since the kinetics of the fastest voltage-gated ion channels can be less than 1 ms.

Members of the group noted that the tissue on which conductivity measurements were made was dead and therefore the conductivity values would not take account of changes resulting from, for example, increases in ion channel activity that occur in living tissue. However, the variation of conductivity with frequency was thought to be of greater significance. It was noted that Gabriel et al (1996) found a four-fold increase in brain conductivity over the frequency range 10 Hz – 100 kHz.

The group noted that the muscle tissue of the heart was an electrical network (syncytium), driven by pacemaker cells situated in the sino-atrial node, and may be expected to show similar weak electric field sensitivity. Reference was made to the (rather inconclusive) work of Graham, Cook and colleagues at the Midwest Research Institute on heart rate variability during EMF exposure (eg Graham et al, 2000a,b). Other relevant tissues capable of network behaviour were thought to include the autonomic and enteric nervous systems (comprising non-myelinated nerve cells, ganglia and plexuses distributed over the body and gut involved in regulating the visceral or 'house-keeping' functions of the body).

Theoretical studies

Several papers by Weaver, Astumian, Adair and colleagues that explored the theoretical limits of biological thresholds to induced electric fields were noted. An early paper (Weaver and Astumian, 1990) suggested a lower limit for detection by membrane macromolecules of 100 $mV\ m^{-1}$. More recently, Weaver et al (1998) calculated a minimum threshold of around 10 $mV\ m^{-1}$ for an elongated cell and Adair et al (1998) suggested

* See, for example, Jefferys et al, 1996; Rubin and Terman et al, 2000; Whittington et al, 2000.

a minimum theoretical sensitivity of 1 mV m^{-1} for systems in which integration of an induced electrical signal takes place over a large number of cells.

Weak electric field effects on the developing CNS

Endogenous direct current (DC) electric fields and currents generated by physiological and metabolic processes within the body can affect nerve growth *in vitro* and *in vivo* and it has been suggested (Nuccitelli, 1992) that they may play an important role in the guidance of normal developmental processes. The potential for induced electric fields to affect the developing nervous system was discussed. The group considered the developing nervous system, both *in utero* and in neonates and young children, as potentially susceptible to induced time-varying electric fields. The considerable number of papers reporting the involvement of DC electric fields of the order of 10–100 V m^{-1} in development of the embryonic and neonatal nervous system and in nerve regeneration was noted (eg AGNIR, 1994; Jefferys, 1995; Rajnicek et al, 1998). Recently, however, Borgens (1999) reported that DC electric fields of only 100 mV m^{-1} can influence the regeneration of nerve fibres in the spinal cord. In addition, Moriarty and Borgens (2001) noted that application of a DC electric field of 320 mV m^{-1} that alternated in polarity every 15 minutes could affect the density and orientation of astrocytes in an injured mammalian spinal cord.

The effect seems to depend to some degree on the surface charge of the substrate, suggesting that the electric current may interact with the way that the neuronal membrane and surface interact. The galvanotropisms may be due to localised membrane depolarisations, caused by the field, leading to calcium influx, which affects growth cone extension (Bedlack et al, 1992). Endogenous electric fields may also play an important role in guiding nerve development and enhancing repair (Borgens, 1982). These reactions all occur for cell depolarisations below the threshold for initiating nerve impulses but it is worth pointing out that spontaneous and stimulus-evoked impulse activities are believed to play a crucial role in local competition between growing axons and the distribution of synaptic boutons on target cells (Shatz, 1990). Any tendency of applied fields to modulate impulse activity could conceivably modify these competitive processes.

Sensitive groups in the population

Epilepsy is characterised by increased neuronal excitability and synchronicity; seizures arise from an excessively synchronous and sustained discharge of a group of neurons (eg Jefferys, 1994; Engelborghs et al, 2000). It was thought to predispose individuals suffering from this disorder as at potentially increased risk from induced electric field effects compared with most individuals. Other characteristics likely to increase sensitivity to weak, induced electric fields include a family history of seizure, the use of tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold and people with serious heart disease or with increased intracranial pressure (Wasserman, 1998). In addition, the potential interference with various medical prosthetic devices was noted.

Voltage-gated ion channels in non-excitable tissues

The group considered that most cells in the body would possess voltage-gated ion channels capable of responding to a weak electric field. Voltage-gated potassium channels are fairly ubiquitous and play a central role in controlling cell membrane

potential; voltage-gated sodium channels are less common but also affect membrane potential (Jan and Jan, 1989). At least four different classes of anion (chloride) channels exist in secretory epithelia, one of which responds to hyperpolarisation, another ubiquitous class is activated by cell-swelling (volume-regulated anion channel) and serves to control cell volume (Nilius and Droogmans, 2001). Generally, many different types of ion channel exist, some of which are voltage sensitive; ion flow through any channel, however, can affect membrane potential generating a signal which can activate other intracellular processes.

Calcium channels are widespread and are particularly important in transducing membrane signals into an increase in the intracellular second messenger [Ca^{2+}] thereby activating many crucial intracellular processes including gene expression. Voltage-gated calcium channels in particular mediate calcium ion entry in response to membrane depolarisation (Catterall, 2000). Typical functions activated by these channels include neurotransmitter release and dendritic Ca^{2+} transients in neurons, excitation-contraction coupling in muscle cells, hormone secretion in endocrine cells (Catterall, 2000), and secretion in other secretory epithelia (Begenisich and Melvin, 1998). Other types of calcium channel, such as calcium-release-activated calcium channels, which also show some voltage dependence, are involved in lymphocyte function (Cahalan et al, 2001). Intracellular Ca^{2+} signalling is also central to many of the functions of vascular endothelial cells, such as the release of vasoactive factors, the regulation of macromolecule transport and endothelial proliferation, and can be modulated by various factors including changes in membrane potential (Nilius and Droogmans, 2001). Such signals have been shown to propagate through gap junctions to neighbouring endothelial cells.

Thus, a variety of cellular functions in 'non-excitable' tissue are likely to respond to changes induced in cell membrane potential by induced electric fields. However, the sensitivity would probably be less than that of excitable cells, the membranes of which provide voltage- and time-dependent non-linearities more likely to amplify small signals. In addition, there will be no integration of these effects over a network of interacting cells comparable to that exhibited by neuronal circuitry.

Conclusions – implications for standards

The group considered that a level of exposure that would avoid potentially adverse effects should be set at the lower end of the recorded thresholds for phosphene induction, which is around 100 mV m^{-1}, possibly as low as 50 mV m^{-1}. It was thought that this should be sufficient to protect normal adults against the potentially adverse effects on the function of the central, autonomic and enteric nervous systems, and on the heart, all of which can be expected to show 'network' behaviour. Other tissues showing voltage-sensitive ion channels are expected to show a lower sensitivity.

Members of the population potentially susceptible to electrical stimulation include people with epilepsy, people with a family history of seizure, or using tricyclic anti-depressants, neuroleptic agents and other drugs that lower seizure threshold, and people with serious heart disease or with increased intracranial pressure. These people should be adequately protected at lower induced electric field strengths, possibly about a factor of five lower than for normal adults. In addition, these values were thought adequate to protect the developing nervous system *in utero*, and in neonates and young children.

It was thought that the appropriate level of exposure would apply over a broad frequency range (approximately 10 Hz – 1 kHz) and that the averaging volume would be based on a minimum of 1000 interacting cells, approximately 1 mm^3 in most nerve tissue. Conversion of the appropriate voltage threshold to a current density threshold depends on knowing the tissue conductivity at the frequency of interest.

Research priorities

Further neurophysiological investigation was recommended, particularly on the sensitivity of network activity for instance on epileptic discharges and physiological oscillations, and on the underlying mechanisms, whether directly on neuronal excitability or on signalling molecules such as nitric oxide. [The current research programme of Professor Jefferys on these effects, funded by the Department of Health, was noted.] The investigation of the threshold and frequency response for these phenomena up to 1 kHz and beyond was considered valuable.

It would also be helpful to identify more rigorously the threshold electric field in the retina for phosphene induction through better dosimetric modelling of relevant volunteer studies. [Professor Blakemore noted that one of his research students was comparing the effects of phosphene induction in the retina by applied electric fields with that induced in the visual cortex by transcranial magnetic stimulation.] In addition, the identification of the responsive elements within the retina to weak induced electric fields was considered useful; this could be achieved relatively easily through neurophysiological investigation.

Further exploration of possible cognitive effects was also considered likely to be of value.

REFERENCES

Adair R K, Astumian R D and Weaver J C (1998). Detection of weak electric fields by sharks, rays and skates. *Chaos,* **8**(3), 576–87.

Adrian D J (1977). Auditory and visual sensations induced by low-frequency electric currents. *Radio Sci,* **12**, 243–50.

AGNIR (1994). Health effects related to the use of visual display units. *Doc NRPB,* **5**(2).

Bedlack R S Jr, Wei M-D and Loew L M (1992). Localised membrane depolarisations and localised calcium influx during electric-field-guided neurite growth. *Neuron,* **9**, 393–403.

Begenisich T and Melvin J E (1998). Regulation of chloride channels in secretory epithelia. *J Membrane Biol,* **163**, 77–85.

Bezzi P, Carmignoto G, Pasti L, Vesce S, Rossi D, Rizzini BL, Pozzan T and Volterra A (1998). Prostaglandins stimulate calcium-dependent glutamate release in astrocytes. *Nature,* **391**(6664), 281–5.

Bezzi P, Domercq M, Brambilla L, Galli R, Schols D, De Clercq E, Vescovi A, Bagetta G, Kollias G, Meldolesi J and Volterra A (2001). CXCR4-activated astrocyte glutamate release via TNFalpha: amplification by microglia triggers neurotoxicity. *Nat Neurosci,* **4**(7), 702–10.

Borgens R (1982). What is the role of natural electric currents in vertebrate regeneration and healing? *Int Rev Cytol,* **76**, 245–98.

Borgens R B (1999). Electrically mediated regeneration and guidance of adult mammalian spinal axons into polymeric channels. *Neuroscience,* **91**(1), 251–64.

Cahalan M D, Wulff H and Chandy K G (2001). Molecular properties and physiological roles of ion channels in the immune system. *J Clin Immunol,* **21**(4), 235–52.

Carpenter R H S (1972). Electrical stimulation of the human eye in different adaptational states. *J Physiol,* **221**, 137–48.

Carstensen E L, Buettner A, Genberg V L and Miller M W (1985). Sensitivity of the human eye to power frequency electric fields. *IEEE Trans Biomed Eng,* **32**, 561–5.

Catterall W A (2000). Structure and regulation of voltage-gated Ca^{2+} channels. *Ann Rev Cell Devel Biol,* **16**, 521–55.

Engelborghs S, D'Hooge R and De Deyn P P (2000). Pathophysiology of epilepsy. *Acta Neurol Belg,* **100**, 201–13.

Estacion M (1991). Characterisation of ion channels seen in subconfluent human dermal fibroblasts. *J Physiol,* **436**, 579–601.

Faber D and Korn H (1989). Electric field effects: their relevance in central neural networks. *Physiol Rev,* **69**, 821–63.

Francis J T, Gluckman B J, Schiff S J (2000). Synchronization between a natural electric field and hippocampal neuronal tissue. *Soc Neurosci Abstr,* **26**, 736.

Gabriel C (1995). Compilation of the dielectric properties of body tissues at RF and microwave frequencies. Report prepared for the NRPB by Microwave Consultants Ltd.

Gabriel S, Lau R W and Gabriel C (1996). The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz. *Phys Med Biol,* **41**, 2251–69.

Gluckman B J, Nguyen H, Weinstein S L and Schiff S J (2001). Adaptive electric field control of epileptic seizures. *J Neurosci,* **21** (2), 590–600.

Graham C, Cook M R, Sastre A, Gerkovitch M M and Kavet R (2000a). Cardiac autonomic control mechanisms in power-frequency magnetic fields: a multistudy analysis. *Environ Health Perspect,* **108**, 737–42.

Graham C, Sastre A, Cook M R, Kavet R, Gerkovitch M M and Riffle D (2000b). Exposure to strong ELF magnetic fields does not alter cardiac autonomic control mechanisms. *Bioelectromagnetics,* **21**, 413–21.

Hassinger T D, Atkinson P B, Strecker G J, Whalen L R, Dudek F E, Kossel A H and Kater S B (1995). Evidence for glutamate-mediated activation of hippocampal neurons by glial calcium waves. *J Neurobiol,* **28** (2), 159–70.

ICNIRP (1998). Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys,* **74** (4), 494–522.

IEEE (2002). Safety levels with respect to human exposure to electromagnetic fields, 0 to 3 kHz. New York, IEEE, IEEE standard C95.6.

Jan L Y and Jan Y N (1989). Voltage-sensitive ion channels. *Cell,* **56**, 13–25.

Jefferys J G R (1994). Experimental neurobiology of epilepsies. *Curr Opin Neurol,* **7**, 113–22.

Jefferys J G R (1995). Nonsynaptic modulation of neuronal activity in the brain: electric currents and extracellular ions. *Physiol Rev,* **75** (4), 689–723.

Jefferys J G R, Traub R D and Whittington M A (1996). Neuronal networks for induced '40 Hz' rhythms. *Trends Neurosci,* **19**, 202–8.

Lawrence J H, Tomaselli G F and Marban E (1993). Ion channels: structure and function. *Heart Disease and Stroke,* **2**, 75–80.

Nilius B and Droogmans G (2001). Ion channels and their role in vascular endothelium. *Physiol Rev,* **81** (4), 1415–59.

Nuccitelli R (1992). Endogenous ionic currents and DC electric fields in multicellular animal tissues. *Bioelectromagnetics,* **Suppl 1**, 147–57.

Parpura V, Basarsky T A, Liu F, Jeftinija K, Jeftinija S and Haydon P G (1994). Glutamate-mediated astrocyte-neuron signalling. *Nature,* **369** (6483), 744–7.

Rajnicek A M, Robinson K R and McCaig C D (1998). The direction of neurite growth in a weak DC electric field depends on the substratum: contributions of adhesivity and net surface charge. *Devel Biol,* **203**, 412–23.

Reilly J P (1998). *Applied Bioelectricity: from Electrical Stimulation to Electropathology.* New York, Springer.

Rubin J and Terman D (2000). Geometric analysis of population rhythms in synaptically coupled neuronal networks. *Neural Computat,* **12**, 597–645.

Saunders R D and Jefferys J G R (2002). Weak electric field interactions in the central nervous system. *Health Phys,* **83** (3), 366–75.

Shatz C J (1990). Impulse activity and the patterning of connections during CNS development. *Neuron,* **5**, 745–56.

Shepherd G M (ed) (1998). *The Synaptic Organisation of the Brain.* Oxford University Press.

Takagi H (2000). Roles of ion channels in EPSP integration at neuronal dendrites. *Neurosci Res,* **37**, 167–71.

Wake K, Tanaka T, Kawasumi M and Taki M (1998). Induced current density distribution in a human related to magnetophosphenes. *Trans IEE Jpn,* **118-A**, 806–11.

Wasserman E M (1998). Risk and safety of repetitive transcranial magnetic stimulation: report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation, June 1996. *Electroenceph Clin Neurophys,* **108**, 1–16.

Weaver J C and Astumian R D (1990). The response of living cells to very weak electric fields: the thermal noise limit. *Science,* **247**, 459–62.

Weaver J C, Vaughan T E, Adair R K and Astumian R D (1998). Theoretical limits on the threshold for response of long cells to weak extremely low frequency electric fields due to ionic and molecular flux rectification. *Biophys J,* **75**, 2251–4.

Whittington M A, Traub R D, Kopell N, Ermentrout B and Buhl E H (2000). Inhibition-based rhythms: experimental and mathematical observations on network dynamics. *Int J Psychophysiol,* **38**, 315–36.

Appendix B

WEAK ELECTRIC FIELDS: DEVELOPMENTS SUBSEQUENT TO APPENDIX A

ICNIRP/WHO Workshop, NRPB, 2003

The report (Appendix A) of an ad hoc expert group that advised NRPB about the potential health effects of physiologically weak electric fields, induced in the body by EMF exposure, stimulated an ICNIRP/WHO workshop held at NRPB in March 2003*. The workshop chair, Professor Blakemore FRS, also chaired the expert group, most members of which also attended the workshop. In addition, the workshop included participants with expertise in biophysics, ion channel function, synaptic function, brain function and cognitive behaviour, cardiac physiology, neuro-endocrinology and developmental biology.

The workshop considerably extended and supplemented the views expressed by the ad hoc expert group both by the presentations and discussion, summarised in the rapporteur's reports, and by the subsequent workshop papers. Many comparable views were expressed. In summary, the main developments to the output of the ad hoc expert group are as follows.

(a) Voltage-gated ion channel properties, pre- and post-synaptic ion channel clustering and neural networks were identified as examples of mechanisms by which physiologically weak but coherent electric signals might be amplified. This effect would be emphasised in convergent pathways, which, for example, characterise the retina and the neuronal input to Purkinje cells in the cerebellum.

(b) Although the retina was still thought a good albeit precautionary model of the sensitivity of central nervous system tissue to induced electric fields, the uncertainties in threshold values and their variation with frequency were emphasised.

(c) Detailed calculation based on neuro-anatomical and physiological considerations suggested a phosphene electric field threshold in the extracellular fluid of the retina to be in the range 10–60 mV m^{-1} at 20–25 Hz (whereas in Appendix A it was expressed as 50–100 mV m^{-1} in retinal tissue).

(d) It was noted that volunteers participating in cognitive studies, which had not produced any clear, unambiguous field dependent effects, had usually been exposed at levels at which the induced electric fields in the brain will have been comparatively low compared to those that induce phosphenes.

(e) The heart, neuroendocrine organs and embryo and fetal development were considered less sensitive to the direct effects of induced electric fields, although it is possible that such effects may be mediated indirectly via interactions with the CNS.

(f) Potentially sensitive individuals were considered to be those with epilepsy and related conditions in which neuronal excitability in the CNS is increased. The greater sensitivity of children regarding electrostimulation was also noted.

* ICNIRP/WHO (2003). Proceedings International Workshop: Weak Electric Field Effects in the Body. *Radiat Prot Dosim,* **106**(4).

Appendix C

SUMMARY OF ICNIRP EXPOSURE GUIDELINES

TABLE C1 *Basic restrictions for time-varying electric and magnetic fields for frequencies up to 10 GHz*

Exposure characteristics	Frequency range	Current density for head and trunk (mA m^{-2}) (rms)	Whole-body average SAR (W kg^{-1})	Localised SAR (head and trunk) (W kg^{-1})	Localised SAR (limbs) (W kg^{-1})
Occupational	Up to 1 Hz	40	–	–	–
	1 Hz – 4 Hz	$40/f$	–	–	–
	4 Hz – 1 kHz	10	–	–	–
	1 kHz – 100 kHz	$f/100$	–	–	–
	100 kHz – 10 MHz	$f/100$	0.4	10	20
	10 MHz – 10 GHz	–	0.4	10	20
General public	Up to 1 Hz	8	–	–	–
	1 Hz – 4 Hz	$8/f$	–	–	–
	4 Hz – 1 kHz	2	–	–	–
	1 kHz – 100 kHz	$f/500$	–	–	–
	100 kHz – 10 MHz	$f/500$	0.08	2	4
	10 MHz – 10 GHz	–	0.08	2	4

Notes

(a) f is the frequency in hertz.

(b) Because of electrical inhomogeneity of the body, current densities should be averaged over a cross-section of 1 cm^2 perpendicular to the current direction.

(c) For frequencies up to 100 kHz, peak current density values can be obtained by multiplying the rms value by $\sqrt{2}$ (~ 1.414). For pulses of duration t_p the equivalent frequency to apply in the basic restrictions should be calculated as $f = 1/(2t_p)$.

(d) For frequencies up to 100 kHz and for pulsed magnetic fields, the maximum current density associated with the pulses can be calculated from the rise/fall times and the maximum rate of change of magnetic flux density. The induced current density can then be compared with the appropriate basic restriction.

(e) All SAR values are to be averaged over any 6-minute period.

(f) Localised SAR averaging mass is any 10 g of contiguous tissue; the maximum SAR so obtained should be the value used for the estimation of exposure.

(g) For pulses of duration t_p the equivalent frequency to apply in the basic restrictions should be calculated as $f = 1/(2t_p)$. In addition, for pulsed exposures in the frequency range from 0.3 GHz to 10 GHz and for localised exposure of the head, in order to limit or avoid auditory effects caused by thermoelastic expansion, an additional basic restriction is recommended. This is that the specific absorption should not exceed 10 mJ kg^{-1} for workers and 2 mJ kg^{-1} for the general public, averaged over 10 g of tissue.

TABLE C2 *Basic restrictions for power density for frequencies between 10 and 300 GHz*

Exposure characteristics	Power density ($W\ m^{-2}$)
Occupational exposure	50
General public	10

Notes

(a) Power densities are to be averaged over any 20 cm^2 of exposed area and any $68/f^{1.05}$-minute period (where f is the frequency in gigahertz) to compensate for progressively shorter penetration depth as the frequency increases.

(b) Spatial maximum power densities, averaged over 1 cm^2, should not exceed 20 times the values above.

TABLE C3 *Reference levels for occupational exposure to time-varying electric and magnetic fields (unperturbed rms values)*

Frequency range	Electric field strength, E ($V\ m^{-1}$)	Magnetic field strength, H ($A\ m^{-1}$)	Magnetic flux density, B (μT)	Equivalent plane wave power density, S_{eq} ($W\ m^{-2}$)
Up to 1 Hz	–	163 000	200 000	–
1 Hz – 8 Hz	20 000	$163\,000/f^2$	$200\,000/f^2$	–
8 Hz – 25 Hz	20 000	$20\,000/f$	$25\,000/f$	–
0.025 kHz – 0.82 kHz	$500/f$	$20/f$	$25/f$	–
0.82 kHz – 65 kHz	610	24.4	30.7	–
0.065 MHz – 1 MHz	610	$1.6/f$	$2.0/f$	–
1 MHz – 10 MHz	$610/f$	$1.6/f$	$2.0/f$	–
10 MHz – 400 MHz	61	0.16	0.2	10
400 MHz – 2000 MHz	$3f^{1/2}$	$0.008f^{1/2}$	$0.01f^{1/2}$	$f/40$
2 GHz – 300 GHz	137	0.36	0.45	50

Notes

(a) f is the frequency as indicated in the frequency range column.

(b) Provided that basic restrictions are met and adverse indirect effects can be excluded, field strength values can be exceeded.

(c) For frequencies between 100 kHz and 10 GHz, S_{eq}, E^2, H^2 and B^2, are to be averaged over any 6-minute period.

(d) For peak values at frequencies up to 100 kHz, see Table C1, note (c).

(e) Between 100 kHz and 10 MHz, peak values for the field strengths are obtained by interpolation from the 1.5-fold peak at 100 kHz to the 32-fold peak at 10 MHz. For frequencies exceeding 10 MHz it is suggested that the peak equivalent plane wave power density, as averaged over the pulse width, does not exceed 1000 times the S_{eq} restrictions, or that the field strength does not exceed 32 times the field strength exposure levels given in the table.

(f) For frequencies exceeding 10 GHz, S_{eq}, E^2, H^2 and B^2 are to be averaged over any $68/f^{1.05}$-minute period (where f is the frequency in gigahertz).

(g) No E-field value is provided for frequencies < 1 Hz, which are effectively static electric fields. Electric shock from low impedance sources is prevented by established electrical safety procedures for such equipment.

TABLE C4
Reference levels for general public exposure to time-varying electric and magnetic fields (unperturbed rms values)

Frequency range	Electric field strength, E ($V\,m^{-1}$)	Magnetic field strength, H ($A\,m^{-1}$)	Magnetic flux density, B (μT)	Equivalent plane wave power density, S_{eq} ($W\,m^{-2}$)
Up to 1 Hz	–	32 000	40 000	–
1 Hz – 8 Hz	10 000	$32\,000/f^2$	$40\,000/f^2$	–
8 Hz – 25 Hz	10 000	$4\,000/f$	$5\,000/f$	–
0.025 kHz – 0.8 kHz	$250/f$	$4/f$	$5/f$	–
0.8 kHz – 3 kHz	$250/f$	5	6.25	–
3 kHz – 150 kHz	87	5	6.25	–
0.15 MHz – 1 MHz	87	$0.73/f$	$0.92/f$	–
1 MHz – 10 MHz	$87/f^{1/2}$	$0.73/f$	$0.92/f$	–
10 MHz – 400 MHz	28	0.073	0.092	2
400 MHz – 2000 MHz	$1.375f^{1/2}$	$0.0037f^{1/2}$	$0.0046f^{1/2}$	$f/200$
2 GHz – 300 GHz	61	0.16	0.20	10

Notes

(a) f is the frequency as indicated in the frequency range column.

(b) Provided that basic restrictions are met and adverse indirect effects can be excluded, field strength values can be exceeded.

(c) For frequencies between 100 kHz and 10 GHz, S_{eq}, E^2, H^2 and B^2 are to be averaged over any 6-minute period.

(d) For peak values at frequencies up to 100 kHz, see Table C1, note (c).

(e) Between 100 kHz and 10 MHz, peak values for the field strengths are obtained by interpolation from the 1.5-fold peak at 100 kHz to the 32-fold peak at 10 MHz. For frequencies exceeding 10 MHz it is suggested that the peak equivalent plane wave power density, as averaged over the pulse width, does not exceed 1000 times the S_{eq} restrictions, or that the field strength does not exceed 32 times the field strength exposure levels given in the table.

(f) For frequencies exceeding 10 GHz, S_{eq}, E^2, H^2 and B^2 are to be averaged over any $68/f^{1.05}$-minute period (where f is the frequency in gigahertz).

(g) No E-field value is provided for frequencies < 1 Hz, which are effectively static electric fields. Perception of surface electric charges will not occur at field strengths less than 25 $kV\,m^{-1}$. Spark discharges causing stress or annoyance should be avoided.

TABLE C5
Reference levels for time-varying contact currents from conductive objects

Exposure characteristics	Frequency range	Maximum contact current (mA)
Occupational	Up to 2.5 kHz	1.0
	2.5 kHz – 100 kHz	$0.4f$
	100 kHz – 110 MHz	40
General public	Up to 2.5 kHz	0.5
	2.5 kHz – 100 kHz	$0.2f$
	100 kHz – 110 MHz	20

Notes

(a) f is the frequency in kilohertz.

(b) These values are set to avoid the possibility of indirect effects of exposure (shock and/or burn).

(c) NRPB notes that equation 11 in the ICNIRP guidelines (ICNIRP, 1998) that deals with the summation for limb current and contact current for multiple frequency sources was subsequently amended (ICNIRP, 1999).

Exposure characteristics	Current (mA)
Occupational	100
General public	45

TABLE C6
Reference levels for current induced in any limb at frequencies between 10 and 110 MHz

Notes

(a) The general public reference level is equal to the occupational reference level divided by √5.

(b) For compliance with the basic restriction on localised SAR, the square root of the time-averaged value of the square of the induced current over any 6-minute period forms the basis of the reference levels.

(c) NRPB notes that equation 11 in the ICNIRP guidelines (ICNIRP, 1998) that deals with the summation for limb current and contact current for multiple frequency sources was subsequently amended (ICNIRP, 1999).

REFERENCES

ICNIRP (1998). Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys*, **74**, 494–522.

ICNIRP (1999). Guidelines on Limiting Exposure to Non-Ionizing Radiation (R Matthes, J H Bernhardt and A F McKinlay, eds). München, ICNIRP 7/99.

Glossary

GUIDELINES TERMINOLOGY

Adverse health effect A biological effect which has a detrimental effect on mental, physical and/or general well being of exposed people, either in the short-term or in the long-term.

Biological effect A measurable change in a biological system in response (for example) to an electromagnetic field.

Caution In this document the terms 'caution' and 'cautious' are used strictly to describe the approach taken in evaluating scientific data and in particular the uncertainties associated with these data and in making judgements as their relevance to exposure restrictions. *See also precaution.*

Direct effect An effect resulting from the interaction of the human body with an electromagnetic field to which it is exposed, eg heating of body tissues.

Dosimetry Evaluation of the absorbed dose or dose rate by an object in an electric, magnetic, or electromagnetic field.

Epidemiology Study of the distribution of disease in populations and of the factors that influence this distribution.

Indirect effect An effect on the human body resulting from the interaction between an electromagnetic field and another object, such as a vehicle or other mechanical structure, with which the body comes into contact, eg shock or burn.

Interference effect An effect on the function of an item of electrical equipment due to interaction with an incident electromagnetic field.

Medicine Study of factors influencing disease in individuals.

Precaution In this document the terms 'precaution' and 'precautionary' are used strictly in relation to possible additional measures that might be considered in the light of the existing limited uncertain evidence of long-term adverse effects of exposure. *See also caution.*

ELECTROMAGNETIC FIELDS

Frequency The number of cycles per second for a periodically varying quantity. Frequency has the unit hertz (Hz).

Electric field strength (E) The force on a stationary unit positive charge at a point in an electric field. The magnitude of the electric field vector (unit $V\ m^{-1}$).

Magnetic flux density (B) The force on a moving unit positive charge at a point in a magnetic field per unit velocity.

Electromagnetic radiation A flow of energy in a given direction and in the form of an electromagnetic wave.

Plane wave A wave such that the corresponding physical quantities are uniform in any plane perpendicular to a fixed direction.

Wavelength (λ) The distance between two successive points of a periodic wave in the direction of propagation at which the oscillation has the same phase.

Power density (S) The power crossing unit area normal to the direction of wave propagation.

Root mean square (RMS) Certain electrical effects are proportional to the square root of the mean value of the square of a periodic function; this is known as the effective value or root mean square value.

Dielectric A class of materials that undergo polarisation.

Specific energy absorption rate (SAR) The rate of absorption of electromagnetic energy per unit body mass, usually expressed in watts per kilogram.

BIOLOGICAL TERMS

Acclimatisation (or acclimation) The physiological changes that occur in response to exposure for a succession of days to an environmental stress, eg heat stress. The changes act to reduce the physiological strain caused by the heat stress of the environment.

Action potential (nerve impulse or 'spike') A sudden brief reversal of the local membrane electrical potential that occurs once a threshold depolarisation has been exceeded and which quickly propagates down a nerve axon conveying 'digitally' encoded information.

Ames test A widely used test to detect possible chemical carcinogens; based on mutagenicity in the bacterium *Salmonella.*

Antigen Any substance, usually (but not always) 'foreign', that provokes an antigen-specific immune response, such as antibody-binding.

Antibody A class of proteins produced by (B) lymphocytes that 'recognises' and binds to a specific antigen, thereby aiding its elimination, or elimination of the agent, such as a bacterium, expressing it.

Apnoea The cessation of breathing.

Apoptosis A specific form of cell death during which cells degrade their own DNA. Apoptosis can occur normally during organ formation, or as a result of DNA or cellular damage.

Atheroma A thickening of the walls of an artery by deposits of fatty substance such as cholesterol.

Atherosclerosis A condition where deposits of fats and minerals form on the wall of an artery and prevent blood from flowing easily (especially important in the aorta and the coronary, renal and cerebral arteries).

Autonomic nervous system A part of the peripheral nervous system that regulates the visceral or 'housekeeping' functions of the body, such as heart-rate and blood pressure. Its cell bodies lie either in the central nervous system, or in ganglia in other parts of the body.

Basophil A type of white blood cell derived from myeloid progenitor cells that, with mast cells, mediate inflammatory immune responses through the release of histamine and other chemicals that cause inflammation.

'Blind' study A study in which the subject or, in the case of studies using animals, tissues or cell cultures, the experimenter, is unaware of whether exposure is to the agent under test or to a neutral or comparison agent until completion of the experiment in order to avoid unconscious subjective bias affecting the study outcome.

Blood–brain barrier A physiological 'barrier' comprising endothelial and epithelial cells that regulates the composition of cerebrospinal fluid of the central nervous system.

Cancer An uncontrolled and abnormal proliferation of cells that causes disease.

Carcinogen An agent that can induce cancer.

Carcinoma – A tumour arising from epithelial tissue (eg glands, breast, skin, linings of the urogenital, intestinal and respiratory systems).

Cell signalling (pathways) A sequence of intracellular changes linking a 'signalling event', such as activation of membrane-bound ion channels or ligand-receptors, and a 'response', such as a change in gene expression, for example, leading to increased proliferation.

Central nervous system Usually taken to mean the cells, such as neurons and glial cells, of the brain and spinal cord. It also includes the retina, which is formed as an outgrowth of the forebrain.

Cerebral thrombosis (an occlusive stroke) A condition where a blood clot enters and blocks a brain artery.

Chromatid One of the two side-by-side replicas ('sister' chromatids) that result from the replication of a single chromosome; their separation during cell division results in two chromosomes.

Chromosome A single molecule of DNA, comprising a large number of genes and other DNA, together with associated protein molecules that condense during cell division to form a deeply staining, rod-shaped body.

Circadian rhythm A rhythmic oscillation of some physiological functions of the body, such as body temperature, which have a periodicity of about 24 hours.

Cognition Information processing by the brain, including processes such as attention, perception, learning, reasoning, comprehending and memory.

Comet assay A single cell electrophoresis assay in which DNA is caused to migrate away from the nucleus by an applied electric field. The extent of migration gives a measure of DNA damage.

Core (or deep) body temperature The 'average' temperature of tissues lying deep within the body, which is normally regulated around a 'set point' value of approximately 37 ± 0.5°C, as distinct from, for example, the temperatures of the skin and peripheral tissues of the limbs, which are more labile.

Coronary thrombosis A blood clot which blocks one of the coronary arteries, leading to a heart attack.

Corticogenesis The growth and development of the cerebral cortex.

Diastole The period of relaxation of heart muscle, following contraction (systole).

Differentiation (cellular) The development of a specialised cellular structure and function from less specialised 'precursor' cells such as stem cells which is generally accompanied by a loss of proliferative capacity.

Disseminated intravascular coagulation A condition characterised by widespread blood clotting in the blood vessels throughout all the organs of the body.

'Double blind' study A volunteer study in which the subject and the experimenter are unaware of until completion of whether exposure is to the agent under test or to a neutral or comparison agent experiment in order to avoid unconscious subjective bias affecting the study outcome.

Electrocardiogram (ECG) A recording of the electrical activity of the heart from electrodes placed on the body.

Electroencephalogram (EEG) A recording of the electrical activity of the brain from electrodes placed on the head.

Electroretinogram (ERG) A recording of the electrical activity of the retina from electrodes placed on the surface of the eye and the head.

Electrotonic 'Graded' non-threshold changes in local membrane electrical potential, usually over the post-synaptic dendritic region and the cell body of a neuron that are generated by excitatory and/or inhibitory inputs from other neurons, which may trigger an action potential to pass down the nerve axon.

Embryo The stage of prenatal development between the fertilised ovum and the completion of major organ development. In humans, this occurs in the first trimester.

Enteric nervous system Comprises the intrinsic neurons of the gut, about the same in number (approximately 100 million) as those of the spinal cord, and which exhibit a high degree of independence from the central nervous system.

Epilepsy Epileptic seizures arise from an excessively synchronous and sustained discharge of a group of neurons; a persistent increase in neuronal excitability is a key feature.

Event-related (or evoked) potential (ERP or EP) A recording of the electrical activity of the brain after a stimulus 'event' such as a visual or auditory stimulus (resulting in VEPs and AEPs, respectively). Late components are associated with cognitive processing.

Fibrillation (ventricular) The loss of organised ventricular contractions of the heart.

Fetus (foetus) The stage of prenatal development between the embryo and birth.

Gene expression The production of a functional protein or an RNA molecule from genetic information (genes) encoded by DNA.

Genotoxin An agent which damages DNA and RNA.

Haematology The study of blood; its formation, its normal composition and function etc and its pathology.

Heat syncope Loss of consciousness due to the heat induced pooling of blood in the dilated vessels of the skin and lower body without an increase in body temperature or cessation of sweating.

Heat exhaustion A heat-related illness characterised by muscular weakness, distress, nausea, vomiting, dizziness, pale clammy skin and fainting, usually associated with lack of heat acclimatisation and physical fitness, low health status and inadequate water intake.

Heat stroke An acute medical emergency arising during exposure to heat from an excessive rise in body temperature and failure of the temperature regulating mechanism. It is characterised by a sudden and sustained loss of consciousness preceded by vertigo, nausea, headache, cerebral dysfunction, bizarre behaviour, and body temperatures usually in excess of 41°C.

Implantation The attachment of the early embryo to the uterine wall.

Intravenous Into a vein.

In vitro 'In glass'; experimental studies of cells or tissues, usually in a sustaining oxygenated, fluid medium.

In vivo 'In life'; experimental studies of processes in living organisms.

'Knockout' organism A genetically modified organism, often a mouse, which has genetic material such a gene stably deleted from its genome.

Leukocyte A white blood cell.

Lymphocyte White blood cells produced in lymphoid tissue that initiate adaptive, antigen-specific immune responses. Some T-lymphocytes are cytotoxic; B-lymphocytes secrete antibodies.

Macrophage A phagocytic cell derived from myeloid progenitor cells found in various tissues.

Malignant Neoplasms or tumours that have become invasive.

Metastasis Tumour cells that leave their site of origin and migrate to other sites in the body.

Microcephaly (or microencephaly) An abnormally small brain.

Micronucleus Chromosome fragments that have not been lost on cell division.

Mutation A stable heritable change in the DNA at a specific site in the in the genome of a cell by an agent (mutagen) such as ionising radiation.

Natural killer (NK) cells Lymphocytes that are not antigen-specific but nevertheless bind to and kill certain tumour and virus-infected cells.

Neonate, neonatal Newly born.

Neoplasm New growth of abnormal tissue.

Neural network Group of interacting neurons.

Neural tube defect A defect of the newly formed precursor of the central nervous system, commonly anencephaly (failure of brain to develop), encephalocele (cyst of the brain), and spina bifida (defects in the closure of the neural tube).

Neurogenesis Proliferation of neural cells to form the nervous system.

Neuron(e) Nerve cell, specialised for the transmission of neural information.

Neurotransmitter A neuroactive substance released by a neuron that causes a post-synaptic response that is relatively quick in onset (less than one millisecond) and short (less than tens of millliseconds) in duration, as distinct from the more prolonged action of neuromodulators.

Neutrophil Phagocytic white blood cells derived from myeloid progenitor cells.

Oncogene A gene which contributes to cancer in a dominant fashion through the mutation and/or abnormal expression of a gene (proto-oncogene) involved in regulating cell proliferation.

Operant behaviour Behaviour, such as pressing a lever, which is 'shaped' by rewards (such as food pellets) or punishment (such as a mild electric shock).

Organogenesis The process of organ formation in developing organisms.

Parturition Birth.

Peripheral nervous system (somatic) The part of the nervous system that mainly deals with the voluntary and conscious aspects of neural control such as voluntary muscle (motor) contraction and sensations such as those of warmth or pressure. The cell bodies lie within the spinal cord, but the peripheral nerves (axons) terminate on muscle fibres or in specialised sensory receptors throughout the body.

Phosphene The perception of flickering light in the periphery of the visual field induced by non-visual means such as a trans-retinal electric current.

Reinforcement (behavioural) An action such as reward or punishment that increases the likelihood of a certain behaviour.

Rapid eye movement (REM) sleep A form of sleep occurring for short episodes and associated with dreaming and brain electrical activity similar to that of alert wakefulness, as distinct from slow-wave sleep which accounts for 75% of sleep time.

Renal insufficiency Reduced function of the kidney.

Respiratory distress syndrome A syndrome of life-threatening progressive pulmonary insufficiency in the absence of known pulmonary disease, usually following a systemic insult such as surgery or major trauma.

Sinus arrhythmia The normal variation of heart rate during the breathing cycle.

Stroke volume The amount of blood pumped out of the ventricle at each heartbeat.

Synapse A junction between two neurons, or between a neuron and a muscle fibre, that allows the transmission of electrical information, usually by means of a chemical transmitter (neurotransmitter) released from the presynaptic terminal of one neuron on to the closely juxtaposed post-synaptic terminal of the other.

Systole The period of contraction of heart muscle following relaxation (diastole).

Teratogen An agent that can cause birth defects.

Thrombosis Blocking of an artery or vein by a blood clot.

Transcription The process whereby RNA is synthesised from a DNA template.

Transcription factor A protein that binds to a DNA sequence with a 'regulatory' function thereby, directly or indirectly, affecting the initiation of transcription.

Transformation Conversion of cells to a state of unrestrained growth in culture, resembling or identical with a tumour-forming (tumorigenic) state.

Transgenic organism A genetically modified organism, often a mouse, which has foreign DNA such as a gene stably integrated into its genome.

Tumour A growth of tissue resulting from abnormal cell proliferation.

Tumour initiator An agent that can produce an initial carcinogenic event such as a mutation.

Tumour progression The process by which initiated and promoted cells become increasingly malignant.

Tumour promoter An agent that can stimulate the proliferation (clonal expansion) of initiated cells.

Tumour suppressor gene A normal cellular gene involved in regulating cell proliferation whose mutation and/or abnormal expression can contribute to cancer in a recessive manner.

Vasoconstriction The contraction of blood vessels, making them narrower.

Vasodilatation (or vasodilation) The relaxation of blood vessels, making them wider.

Vigilance tasks Responding to unusual and infrequent stimuli (signals) occurring against a background of usual and frequent stimuli (events). Vigilance can be either visual or auditory.

Voltage-gated ion channel Cell membrane proteins that allow the passage of particular ion species across the cell membrane in response to the opening of a molecular 'gate' which is steeply sensitive to the transmembrane voltage. They are associated with electrical excitability.

Wild-type (gene) The gene that is found in nature or in the standard laboratory stock for a given organism.

Working memory An active system for temporarily storing and manipulating information needed in the execution of complex cognitive tasks.

EPIDEMIOLOGICAL TERMS

Bias A systematic tendency to error as a consequence of the design or conduct of a study.

Case–control study An investigation into the extent to which a group of persons with a specific disease (the cases) and comparable persons who do not have the disease (the controls) differ with respect to exposure to putative risk factors.

Cohort study An investigation involving the identification of a group of individuals (the cohort) about whom certain exposure information is collected, and the ascertainment of occurrence of diseases at later times. For each individual, information on prior exposure can be related to subsequent disease experience. Cohort studies may be conducted prospectively or retrospectively. *See retrospective study*.

Combined analysis Analysis of data pertaining to the same topic that have been collected in several different studies. Usually based on individual level data from each of the available studies, rather than on the published findings. *See meta-analysis*.

Confidence interval (CI) An interval calculated from data when making inferences about an unknown parameter. In hypothetical repetitions of the study, the interval will include the parameter in question on a specified percentage of occasions (eg 90% for a 90% confidence interval).

Confounding Spurious findings due to the effect of a variable that is correlated with both the exposure and disease under study.

Meta-analysis Analysis of data pertaining to the same topic that have been collected in several different studies. Usually refers to an analysis based on published findings from individual studies, rather than on the original data sets. *See combined analysis*.

Non-differential measurement errors Errors in exposure assessment that do not depend on whether or not someone develops the disease under study.

Prospective study An epidemiological study in which data on exposures and disease outcome are collected as the events occur, unlike a retrospective study (*see below*). Some cohort studies are conducted prospectively.

Relative risk The ratio of the disease rate in the group under study to that in a comparison group, with adjustment for confounding factors such as age, if necessary.

Retrospective study An epidemiological study in which data on exposures and disease outcome are collected some time after the event, unlike a prospective study (*see above*). Examples include case–control studies and some cohort studies.

Significance level The probability of obtaining a result at least as extreme as that observed in the absence of a raised risk. A result that would arise less than 1 in 20 times in the absence of an underlying effect is often referred to as being 'statistically significant'.

Statistical power The probability that, with a specified degree of confidence, an underlying effect of a given magnitude will be detected in a study.