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6 Effects of Electromagnetic Fields on Organs and Tissues

Introduction

A large body of literature exists on the response of tissues to electromagnetic fields, primarily in the extremely-low-frequency (ELF) and microwave-frequency ranges. In general, the reported effects of radiofrequency (RF) radiation on tissue and organ systems have been attributed to thermal interactions, although the existence of nonthermal effects at low field intensities is still a subject of active investigation. This chapter summarizes reported RF effects on major physiological systems and provides estimates of the threshold specific absorption rates (SARs) required to produce such effects. Organ and tissue responses to ELF fields and attempts to characterize field thresholds are also summarized. The relevance of these findings to the possible association of health effects with exposure to RF fields from GWEN antennas is assessed.

Nervous System

The effects of radiation on nervous tissues have been a subject of active investigation since changes in animal behavior and nerve electrical properties were first reported in the Soviet Union during the 1950s and 1960s.[1] RF radiation is reported to affect isolated nerve preparations, the central nervous system, brain chemistry and histology, and the blood-brain barrier.

In studies with in vitro nerve preparations, changes have been observed in the firing rates of Aplysia neurons and in the refractory period of isolated frog sciatic nerves exposed to 2.45-GHz microwaves at SAR values exceeding 5 W/kg.[2,3,4] Those effects were very likely associated with heating of the nerve preparations, in that much higher SAR values have not been found to produce changes in the electrical properties of isolated nerves when the temperature was controlled.[5, 6] Studies on isolated heart preparations have provided evidence of bradycardia as a result of exposure to RF radiation at nonthermal power densities,[7] although some of the reported effects might have been artifacts caused by currents induced in the recording electrodes or by nonphysiological conditions in the bathing medium.[8,9,10] Several groups of investigators have reported that nonthermal levels of RF fields can alter Ca^{2+} binding to the surfaces of nerve cells in isolated brain hemispheres and neuroblastoma cells cultured in vitro (reviewed by the World Health Organization[11] and in Chapters 3 and 7 of this report). That phenomenon, however, is observed only when the RF field is amplitude-modulated at extremely low frequencies, the maximum effect occurs at a modulation frequency of 16 Hz. A similar effect has recently been reported in isolated frog hearts.[12] The importance of changes in Ca^{2+} binding on the functional properties of nerve cells has not been established, and there is no clear evidence that the reported effect of low-intensity, amplitude-modulated RF fields poses a substantial health risk.

Results of in vivo studies of both pulsed and continuous-wave (CW) RF fields on brain electrical activity have indicated that transient effects can occur at SAR values exceeding 1 W/kg.[13,14] Evidence has been presented that cholinergic activity of brain tissue is influenced by RF fields at SAR values as low as 0.45 W/kg.[15] Exposure to nonthermal RF radiation has been reported to influence the electroencephalograms (EEGs) of cats when the field was amplitude-modulated at frequencies less than 25 Hz, which is the range of naturally occurring EEG frequencies.[16] The rate of Ca^{2+} exchange from cat brain tissue in vivo was observed to change in response to similar irradiation conditions.[17] Comparable effects on Ca^{2+} binding were not observed in rat cerebral tissue exposed to RF radiation,[18] although the fields used were pulsed at EEG frequencies, rather than amplitude-modulated. As noted above, the physiological significance of small shifts in Ca^{2+} binding at nerve cell surfaces is unclear.

A wide variety of changes in brain chemistry and structure have been reported after exposure of animals to high-intensity RF fields.[19] The changes include decreased concentrations of epinephrine, norepinephrine, dopamine, and 5-hydroxytryptamine; changes in axonal structure; a decreased number of Purkinje cells; and structural alterations in the hypothalamic region. Those effects have generally been associated with RF intensities that produced substantial local heating in the brain.

Extensive studies have been carried out to detect possible effects of RF radiation on the integrity of the blood-brain barrier.[20,21] Although several reports have suggested that nonthermal RF radiation can influence the permeability of the blood-brain barrier, most of the experimental findings indicate that such effects result from local heating in the head in response to SAR values in excess of 2 W/kg. Changes in cerebral blood flow rate, rather than direct changes in permeability to tracer molecules, might also be incorrectly interpreted as changes in the properties of the blood-brain barrier.

Effects of pulsed and sinusoidal ELF fields on the electrical activity of the nervous system have also been studied extensively.[22,23] In general, only high-intensity sinusoidal electric fields or rapidly pulsed magnetic fields induce sufficient current density in tissue (around 0.1-1.0 A/m^2 or higher) to alter neuronal excitability and synaptic transmission or to produce neuromuscular stimulation. Somewhat lower thresholds have been observed for the induction of visual phosphenes (discussed in the next section) and for influencing the electrical activity of Aplysia pacemaker neurons when the frequency of the applied field matched the endogenous neuronal firing rate.[24] Those effects, however, have been observed only with ELF frequencies and would not be expected to occur at the higher frequencies associated with GWEN transmitters. Recent studies with human volunteers exposed to 60-Hz electric and magnetic fields with intensities comparable with those of high-voltage power lines have shown no consistent effects on the EEG.[25] Minor changes were observed in reaction time and heart rate, but the variations were within normal ranges.

Visual System

Cataract development as a result of exposure of the eye to high-intensity RF radiation has been studied for more than 30 years. Extensive experiments have been carried out with rabbits to determine the dependence of cataractogenesis on the frequency and intensity of RF fields and on exposure time.[26-28] In general, the lowest thresholds for cataract induction have been observed with near-field exposure at 1-10 GHz, and a power density greater than 100 mW/cm^2 applied for at least an hour is required. Most of the evidence indicates that the mechanism of injury leading to lens opacity is thermal, and pulsed and CW microwave fields appear to have similar thresholds for producing cataracts.[19] Multiple subthreshold exposures do not lead to cataracts if the time between exposures is long enough to permit the tissue to return to its normal temperature.[1] At frequencies where the wavelength of the RF field is not well matched to the dimensions of the eye, cataracts are not produced even at extremely high power densities approaching the lethal levels. Although it is difficult to extrapolate results from laboratory animals to humans, the threshold power density required to produce cataracts is expected to be similar in rabbits and humans because of the structural similarities and comparable dimensions of the eyes in these species.

Results of recent studies with monkeys have indicated that vascular leakage can increase at relatively low power densities of pulsed 2.45-GHz radiation when the eye is pretreated with timolol maleate, which decreases intraocular pressure by reducing the production of aqueous humor. A power density as low as 1 mW/cm^2, corresponding to an intraocular SAR of 0.26 W/kg, has been observed to produce the effect.[29] Those findings might have implications for RF ocular damage in humans being treated with timolol maleate for glaucoma. However, the threshold power density at 2.45 GHz is still well in excess of the intensity of the RF fields produced by GWEN antennae in areas accessible to the general public.

A visual phenomenon associated with exposure to ELF fields that has been studied for nearly a century is the induction of a flickering illumination known as phosphenes. Time-varying magnetic fields with either pulsed or sinusoidal waveforms and frequencies below 100 Hz have been shown to produce phosphenes when the time rate of change of the field exceeds 1.3 T/sec.30 The frequency most likely to produce magnetophosphenes with sinusoidal fields is 20 Hz; the threshold flux density for eliciting the visual effect is 8 mT.[31] A similar frequency dependence has been observed for electrophosphenes produced by placing electrodes in contact with the forehead near the eyes.[32] The locus of the effect is in the retina, and available evidence suggests that induced currents in the retina elicit visual responses similar to those resulting from photic stimulation.[30] Changes in visually evoked potential (VEP) have also been reported in response to ELF magnetic fields with flux densities that are 5-10 times greater than those required to produce phosphenes.[3] Because phosphenes and VEP alterations are observed only with fields below 100 Hz, such phenomena are not expected to occur in response to the low-frequency fields associated with GWEN antenna.

Endocrine System

Many studies with rodents and monkeys have demonstrated that exposure to thermogenic levels of RF radiation produces endocrine alterations, the most consistent change being an increase in plasma corticosterone.[1, 34] SAR values in excess of 3 W/kg produce an increase in plasma corticosterone in rats that depends on secretion of adrenocorticotropic hormones by the pituitary.[35] Decreased thyroid hormone levels have also been observed in response to thermogenic levels of RF radiation, and this response has been associated with an inhibition of thyrotropin secretion by the pituitary.[36,37] In general, the alteration of hormone concentrations is reversible after termination of the RF exposure. Those findings indicate that RF heating alters the complex interactions of the hypothalamic, pituitary, adrenal, and thyroid systems that are important in the maintenance of homeostasis.[19] It is noteworthy that a 2-yr exposure of rats to nonthermogenic pulsed 2.45-GHz microwaves did not produce detectable endocrine alterations.[37]

Studies on the possible endocrine effects of ELF electric and magnetic fields have yielded inconsistent results.[22] Increases, decreases, and no change in plasma steroid hormones have been reported. Results of studies with dogs and rats suggest that the threshold 60-Hz electric field required to produce changes in blood concentrations of corticosterone or testosterone is in excess of 10 kV/m.[38-40] Results of experiments with monkeys exposed to 60-Hz electric and magnetic fields at intensities typical of those in the vicinity of high-voltage transmission lines indicated that a decrease in neurotransmitter concentrations occurs during chronic exposure.[41] However, there were no other observations of behavioral or physiological changes in the exposed animals.

The most widely studied effect of ELF fields on the endocrine system is an apparent depression in the nocturnal rise of pineal melatonin.[42] Changes in pineal melatonin have reportedly occurred after 2-3 wk of exposure to electric fields with intensities exceeding 1.7 kV/m in air. The effect is reversible, with a return of nocturnal pineal melatonin to control values within 3 d of termination of exposure. A similar effect on pineal melatonin has been observed after exposure of rodents to a 0.05 mT static magnetic field that was continuously switched on and off in 5-min cycles for 1 h beginning 3.5 h after the onset of darkness.[43] Interest in this phenomenon has centered around the effects of melatonin on cell proliferation and its possible carcinostatic effects.[44-46] A major problem in the interpretation of the results of studies is lack of quantitative information on the threshold fields required to alter melatonin concentration. It is also unclear whether ELF fields directly alter pinealocyte functions or whether the reported alteration in pineal melatonin production is secondary to effects of the fields on the nervous system. Further studies are needed to assess the possible influence of field-induced changes in pineal melatonin on physiological regulation and the risk of endocrine-dependent cancers. It is not now possible to extrapolate the available information obtained with 60-Hz fields or intermittent DC magnetic fields to the possible effects of fields with higher frequencies.

Immune System

Effects of RF-field exposure on cellular components of the immune system have been reported with both in vitro and in vivo test systems.[1] Lymphoblast transformation and changes in responsiveness to mitogens have been reported, although the effects observed in different laboratories have been quite variable. It appears from available information that the threshold SAR for altering lymphocyte responses to mitogens exceeds 4 W/kg with both pulsed and CW microwaves.[47-49] Thermogenic levels of exposure have been found to decrease natural killer cell activity and to activate macrophages.[50, 52] The changes observed in components of the immune system at RF power densities that produce tissue heating are consistent with the expected effects of increased release of steroid hormones into the circulation.[1,52,53] In one study involving a 2-yr exposure of rats to a nonthermal level of pulsed 2.45-GHz microwaves (SAR, 0.4 W/kg), no significant irreversible changes were found in the concentrations of lymphocytes or their responses to mitogen stimulation.

Numerous studies have been carried out to determine the effects of ELF electric and magnetic fields on components of the immune system. In general, sinusoidal ELF fields have been found to have no significant effects on immune competence after in vivo exposure of laboratory animals.[22,25] However, reduced mitogen responses and decreased target-cell toxicity have been reported for lymphocytes exposed in vitro to pulsed magnetic fields or 60-Hz amplitude-modulated RF fields.[55-57] These effects might have resulted from the relatively high current densities induced in the cell suspensions. In a study involving 60-Hz electric and magnetic fields with a sinusoidal waveform and intensities comparable with those of the fields near high-voltage power lines, no effects were observed on the immunologic functions of peripheral human and canine lymphocytes obtained from donors that either were normal or had been challenged with specific antigens.[58]

Hematologic and Cardiovascular Systems

Several studies have been performed to assess the effects of both thermogenic and nonthermogenic levels of RF radiation on blood chemistry and blood-cell counts.

Most were conducted with 2.45-GHz microwaves, and the results indicate that power densities producing an average whole-body SAR of less than 2.5 W/kg do not produce significant alterations in hematologic indexes.[59] In one chronic-exposure study with rabbits subjected to 2.45-GHz microwaves 23 h/d for 180 d, a small decrease was observed in eosinophil count, serum albumin concentration, and calcium concentration.[60] None of the other 38 blood characteristics measured in the study were found to change in response to chronic RF exposure.

At high levels of RF exposures of mice leading to rectal temperature increases of 2-4ºC, decreased lymphocyte counts and increased neutrophil counts were observed.[61] It was suggested that the release of adrenal steroids into the blood as a result of heat stress could have produced the changes in blood-cell counts.[52,53] Thermogenic levels of pulsed or CW microwaves might also affect the cellular composition and proliferative capacity of bone-marrow cells.[62,63] Both bradycardia and tachycardia have been observed in laboratory animals exposed to thermogenic levels of RF radiation with SAR values in excess of 2.5 W/kg.[64,65] In general, the effects on cardiac dynamics were transient and consistent with effects expected from body heating.

As reviewed by several authors,[22,54, 66] the threshold ELF fields for producing significant cardiovascular and hematologic alterations are high. For example, cardiovascular indexes were not affected by exposure to 60-Hz, 100-kV/m fields.[67] Acute human exposures to ELF electric fields up to 200 kV/m and magnetic fields up to 5 mT have also failed to show any consistent hematologic or cardiovascular effects.[68,69]

Animal Carcinogenesis

A few studies have investigated the carcinogenic potential of microwave radiation in whole animals. Male Swiss albino mice were exposed to a radar transmitter with 9.27-GHz frequency modulated with 2-μsec pulses at a pulse repetition frequency of 500/sec for 59 wk, 5 d/wk and 4.5 min/d.[70] The power used (1 kW/m^2) caused a temperature rise of 3.3ºC. There was no difference between exposed and control animals in a number of characteristics examined, including body weight, red-cell and white-cell counts, and body temperature. Testicular degeneration occurred in 23 of 57 (40%) of treated animals and in 3 of 37 (8.1%) of the controls. Monocytic or lymphatic organ tumors or myeloid leukemia was seen in 21 of 60 (35%) treated and 4 of 40 (10%) control animals. However, that increase was seen in the animals killed at 16 mo—I mo after cessation of treatment—but not at 19 mo. In addition, there has been considerable criticism of the experimental methods (e.g., definition of leukosis as an increase in circulating leukocytes, which could have been due to infection) and statistical analysis.[71, 72] Thus, the study is of questionable use for supporting an increase in cancer risk. The incident power density was approximately 100 times greater than the highest relevant GWEN levels.

Female RFM mice were exposed to 0.8-GHz microwave radiation for 2 h/d, 5 d/wk for 35 wk at 430 W/m.[73] Red and white cell counts, hemoglobin, hematocrit, activity, body weight, and survival were measured, but no histopathologic examinations, were carried out. The only statistically significant finding was an increase in body weight of animals older than 86 wk in exposed mice over control animals.

A University of Washington study on male Sprague-Dawley rats was designed to simulate the maximum absorbed power (0.4 W/kg) of 0.45-GHz radiation.[74] The frequency was chosen as typical of a midrange radar system. Rats were exposed at 2.45 GHz, because it yielded a ratio of wavelength to maximum body dimension similar to that of children exposed at 0.45 GHz. Benign pheochromocytoma of the adrenal medulla was the only lesion with a statistically significant increase in incidence. However, that incidence was not higher than that seen in control rats of other colonies. The time for appearance of first tumor was also shorter in treated animals (457 d) than in control animals (540 d). When all malignant tumors observed at all sites are combined, there is a statistically significant increase in incidence in the exposed animals. That holds true for carcinomas, but not for sarcomas.

An effect on the process of carcinogenesis has been reported in several studies that used injected tumor cells or animals treated with low doses of a known carcinogen. The effects of 2.45-GHz microwave radiation at 50 and 150 W/m2 in an anechoic chamber was determined.[75] Lung sarcoma cells were injected intravenously into Balb/C mice, and the lung-cancer colonies were counted after 1, 2, and 3 mo of treatment. After 3 mo, the numbers of lung nodules were 3.6 ±2.2. 7.7 ± 2.0, 6.1± 8, and 10.8 ± 2.1 in control animals, chronically stressed animals, animals exposed at 50 W/m^2, and animals exposed at 150 W/m^2, respectively. The time to appearance of spontaneous breast tumors in 50% of C3H/HeA mice decreased in animals treated with chronic stress, 50 W/m^2, and 150 W/m^2 (255, 261, and 219 d, respectively, compared with 322 d in controls). The time of appearance of skin tumors induced by benzo[a]pyrene was also shortened when irradiation for 1 or 3 mo preceded carcinogen application or when radiation and carcinogen were given at the same time.[75] Again, stress closely duplicated the effect of 50-W/m^2 radiation, and, although the results of 150 W/m^2 were significantly greater than those of stress or 50 W/m^2, thermal effects might be responsible for the results at 150 W/m^2. The power density of 50 W/m^2 is approximately 7 times the low-frequency power density at the GWEN site boundary.

Negative and beneficial results of exposure have also been reported. The effect of continuous or pulsed waves of 2.45 GHz (10 W/m^2; SAR, 1.2 W/kg) was studied in black C57/6J mice with B16 melanoma.[76] No significant effects on tumor development or survival times were observed. Beneficial effects of induced hyperthermia have been observed after treatment with microwave radiation.[77,78] Lung sarcoma cells injected into Balb/C mice demonstrated temporary regression after exposure to 2.45-GHz radiation. After radiation exposure was stopped, tumor volumes increased and lung metastases exceeded those in untreated animals.[77] Sarcoma cells were implanted on postpartum day 16 into CFW mice that had been irradiated in utero with 2.45-GHz microwaves (35 W/kg) during days 11-14 of gestation; the mice were then subjected to additional exposure to microwave radiation. Fetal exposure to radiation that increased the dam's colonic temperatures by an average of 2.2ºC decreased tumor incidence (13%, with 46% in controls). Both tumor-bearing and tumor-free animals that were irradiated as fetuses lived longer, on the average, than controls. Enhanced immunocompetence related to increases in temperature was suggested as an explanation.

In summary, several studies have provided some evidence of possible carcinogenic potential, and others have shown no effect. Consistent reproducible studies demonstrating a dose-response relation in animals are lacking, and the interpretation of several studies is complicated by thermally induced stress. All studies were conducted with electromagnetic fields larger than the relevant GWEN fields.

Considerable interest has arisen concerning a possible role of electromagnetic fields as cocarcinogens or cancer promoters. Results of cellular studies that support such speculation are discussed in Chapter 7. Studies by McLean et al.[79] have begun to explore directly the possible role of 60-Hz magnetic fields as cancer promoters. In their studies, cancers in SENCAR mice—known for their sensitivity to the promoting effects of 12-O-tetradecanoylphorbol-13-acetate (TPA)—were initiated with dimethylbenzanthracene and then promoted with TPA, a 2-mT magnetic field, or a combination of TPA and a magnetic field. Tumor development was then observed for 20 wk. There was no significant difference in tumor development between those promoted with TPA alone and those promoted with TPA and a magnetic field. However, recent results of another experiment by the same group of investigators suggest that a 60-Hz magnetic field acts as a co-promoter. Additional studies are required to substantiate those findings. Beniashvili et al.[80] treated rats with nitrosomethyl urea and then exposed them to either a 0.2 G static or 50-Hz magnetic field for either 0.5 or 3 h/d for up to two years. They found an increased incidence and number of mammary tumors in the groups exposed to the magnetic fields, with the ac field being more active than the static one. They also reported an increased tumor response in rats exposed to the 50-Hz field alone.

Conclusions

Very few studies have been performed on the responses of organs and tissues to electromagnetic fields in the low-frequency or ultra-high-frequency ranges used by GWEN transmitters, but it is possible to conclude from the analysis presented here that effects of RF radiation are unlikely to occur at the power densities and absorbed energies associated with GWEN fields. The possible existence of nonthermal effects—such as the reported effects of low-intensity, amplitude-modulated RF fields on Ca^{2+} binding in nerve tissue—do not alter that conclusion, in that the waveforms and frequency spectra of these fields are different from those of the GWEN fields. Physiologic effects of ELF fields—with frequencies less than one five-hundredth those of GWEN fields—are generally associated with high field intensities and large induced-current densities in tissue. Some physiologic effects of ELF fields that might result from low induced current in tissue, such as alterations in pineal melatonin concentration, have not been shown to pose a direct risk to human health. In sum, studies on physiologic effects of ELF fields have yielded little evidence that exposure to the low-frequency fields from GWEN antennae in areas of most likely public access would represent a health risk.

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