Radiofrequency Fields and Teratogenesis

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Experimental studies that sought teratologic effects or developmental abnormalities from exposure to radiofrequency electromagnetic fields (RFEMF) in the range 3 kHz–300 GHz are critically reviewed for their possible consequences on human health. Those studies were conducted on beetles, birds, rodents, and nonhuman primates. Collectively, those experimental studies indicate that teratologic effects can occur only from exposure levels that cause biologically detrimental increases in body temperature. No reliable experimental evidence was found for nonthermal teratologic effects; rodents, mouse fetuses, and perinatal mice are more susceptible to such effects than rats. The primary confirmed effect in rats at high RFEMF levels was initial weight deficits in fetuses and neonates that decreased with infant growth. More generally from findings with pregnant mammals, exposures at RFEMF levels far higher than those permitted under the IEEE human exposure guidelines are necessary to reach or exceed cited experimental thresholds for maternal temperature increases. Some results indicated that the levels necessary to cause such effects in pregnant mammals could exceed those lethal to the dams. In a behavioral study of squirrel monkeys, no effects were observed on usual dam-offspring interactions or EEGs, but unexpected deaths of a number of offspring had occurred. However, this finding was not confirmed in a study solely on infant death using a larger number of subjects for greater statistical validity. Also reviewed were epidemiologic studies of various human populations considered to have been chronically exposed to environmental levels of RFEMF. Early studies on the incidence of congenital anomalies yielded no credible evidence that chronic exposure of pregnant women or of fathers exposed to RFEMF from nearby sources at levels below those guidelines would cause any anomalies in their offspring. The findings of studies on pregnancy outcomes of female physiotherapists occupationally exposed while treating patients with RFEMF were mixed, but taken collectively, the findings were negative. Bioelectromagnetics Supplement 6:S174–S186, 2003.

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INTRODUCTION

In a narrow sense, teratology refers to the study of anatomical aberrations (terata) in developing fetuses, but more generally includes fetal death and/or resorption, as well as postpartum physiological and developmental abnormalities. The fetus is acknowledged to be especially sensitive to changes in environmental conditions. Embryonic tissues grow rapidly and specialize, so perturbations in the embryonic environment could lead to changes in cell proliferation and differentiation. Such effects could be due to internal chemical or physical mechanisms or could be ascribed to exposure to various external agents.

This review discusses studies of the effects of exposure to nonionizing electromagnetic fields as the external agent and in particular, fields in the frequency range 3 kHz–300 GHz that are of specific interest to Subcommittee 4 (SC4) of IEEE International Committee on Electromagnetic Safety [IEEE, 1999]. This body is engaged in revising its 1991/1999 guidelines for maximum allowable human exposure to such fields. For convenience, the acronym for radiofrequency electromagnetic fields, “RFEMF,” is used here to indicate that nominal frequency range.

Of much concern are any potential teratologic effects of RFEMF on humans. For moral and legal considerations, such effects were investigated experimentally in a number of mammalian species as surrogates for humans. Also assessed here were the findings and limitations of various epidemiologic studies of groups known to have been occupationally exposed to RFEMF.

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or of members of the general public presumed or known to have undergone such exposure by being in the general or immediate vicinity of various types of RFEMF emitters.

This paper was derived in part from a comprehensive review of the topic [Heynick and Polson, 1996], in which the authors had critically assessed the quality of the biological and engineering methodology as well as the experimental findings presented in each paper. Emphasized in this shorter paper are the experimental aspects and findings on several common mammalian species. In addition, several early investigations with nonmammalian species, mostly insects and birds, are briefly discussed, mostly for historical reasons.

NONMAMMALIAN SPECIES

Darkling Beetle

Several early teratology studies were performed in which pupae of *Tenebrio molitor* (darkling beetle) were exposed to RFEMF at various levels for varying durations. Carpenter and Livstone [1971] exposed pupae to 10 GHz RFEMF for 2 h at 17 mW/cm² [specific absorption rate (SAR) = 40 W/kg] or for 20–30 min at 68 mW/cm² (SAR = 160 W/kg). About 90% of the sham exposed pupae developed normally. For comparison, only about 20% of the those exposed at 17 mW/cm² developed into normal beetles, about 4% died, and about 76% exhibited gross abnormalities. It is noteworthy that exposure for 20 min at 68 mW/cm² yielded about 4% more live beetles, 21% fewer dead beetles, and 25% fewer gross abnormalities. Also for comparison, about 75% of the pupae heated conventionally to the temperature produced at 17 mW/cm² emerged as normal beetles, findings that led these authors to conclude that the abnormal development of RFEMF exposed pupae was not a thermal effect.

Lindauer et al. [1974] exposed pupae at 9 GHz (CW or pulsed) at 8.6 or 17.1 mW/cm² (21 or 41 W/kg) for 2 h. Several RFEMF related differences between exposed and control beetles were significant, but with no clear dependence of effect on dose rate or total dose. No significant differences in results were evident between pulsed and CW RFEMF at the same average power density. Green et al. [1979] also reported significant numbers of dead or deformed beetles from exposure to levels in the range 0–34 mW/cm², mostly related to temperature rises. Susceptibility to damage was higher for those treated at relative humidities less than 35% than at higher humidities.

Pickard and Olsen [1979] indicated that the findings among the studies above and their differences were likely due to nonRFEMF confounding factors. These researchers studied pupae grown with larvae from two different sources and fed them differently. Larvae obtained from one supplier were raised on Purina dairy meal while larvae from another supplier were raised on Kellogg’s Special K. No significant differences were found in incidences of gross abnormalities between pupae from either source exposed to an E field at the equivalent of 130 W/kg and their control pupae. However, there were more abnormal beetles in the controls fed Special K than in the Purina fed controls. In a subsequent study with accurate dosimetric measurements, Olsen [1982] found that incidences of anomalies were temperature dependent, with a hyperthermia threshold at 40 °C. Clearly then, teratogenic effects in *Tenebrio* were thermally induced and not nonthermal in etiology.

Birds

Over the past quarter century, numerous studies of the effects of RFEMF on several avian species had been conducted. Endpoints included hatchability, hatchling weights, viability, and incidences of abnormalities. In general, the findings showed no significant differences between exposed and sham exposed eggs in any endpoints except when the exposure levels were high enough to increase internal egg temperatures by a few degrees above normal incubation temperatures.

Hills et al. [1974] exposed arrays of chicken or turkey eggs in several stages of development to 2.45 GHz RFEMF at “high” power and reported reduced hatchability or failure to hatch. However, no information on exposure methodology or dosimetry was given. Fisher et al. [1979] exposed chicken egg arrays to 2.45 GHz at about 4 mW/cm² and observed delays in embryo development, but the spatial range of power densities over each egg array was large (1.4–6.2 mW/cm²), with the likelihood of large variations in internal egg temperature in each array. Saito et al. [1991] exposed arrays of chicken eggs to 428 MHz RFEMF and observed lower hatchabilities in the exposed eggs compared to sham exposed eggs. However, the spatial SAR range over the arrays was also large (3.1–33.0 W/kg).

Numerous studies of RFEMF effects on Japanese quail eggs were performed [Hamrick and McRee, 1975; McRee et al., 1975; Hamrick et al., 1977; Inouye et al., 1982a; McRee et al., 1983; Byman et al., 1985; Gildersleeve et al., 1987; Spiers and Baummer, 1991]. All of those studies were done with 2.45 GHz RFEMF at estimated SARs in the range 3.2–25 W/kg. The endpoints included hatchability, hatchling weights, viability, and incidences of abnormalities. The results showed no significant differences between RFEMF and sham exposed eggs in any endpoints unless the ex-
exposures were high enough to raise internal egg temperatures by a few degrees above normal incubation temperatures.

**MAMMALIAN SPECIES**

**Mice**

Among the early RFEMF related studies on teratogenesis in mice was that of Bollinger et al. [1974], who investigated the effects of exposure to 25 kHz on growth and reproduction. The exposures were to orthogonal electric and magnetic fields at 15 kV/m and 7.5 A/m. The results showed no statistically significant effects on growth, reproductive ability, or metabolism of the neonates or on the growth of their eventual offspring.

Rugh et al. [1974, 1975] exposed unrestrained timed-mated pregnant mice on gestation day 8.5 to 2.45 GHz RFEMF at 123 mW/cm² (SAR about 110 W/kg) for 2–5 min. The dams were euthanized on day 18 and the fetuses were examined for resorptions and anomalies. The authors stated that they could not find a threshold for teratogenesis. The data were obscure, rendering it difficult to assess their validity. However, an independent reanalysis of their data [Heynick and Polson, 1996] indicated that there was a threshold of about 13 J/g for exencephaly and resorptions. For unclear reasons, Rugh et al. did not study control mice, but in a similar study by Chernovetz et al. [1975] with C3H/HeJ mice (discussed next), about 20% of the fetuses from their control dams were abnormal.

Chernovetz et al. [1975] exposed groups of pregnant C3H/HeJ mice to 2.45 GHz for 10 min (SAR ~38 W/kg) on gestation days 11, 12, 13, and 14. The dams were euthanized on day 19, at which time the numbers of implantations and resorptions were counted and the fetuses were examined for abnormalities. They observed no significant differences between the RFEMF and sham groups in the percentages of normal or abnormal fetuses, and no dependence on gestation day of treatment. Based on their data, the authors indicated that teratogenesis would occur in pregnant mice only at levels close to lethality for the dams.

Berman et al. [1978] exposed pregnant CD-1 mice to 2.45 GHz for 100 min daily on gestation days 1 through 17 at power densities in the range 3.4–28 mW/cm² (SARs up to 8 W/kg). On day 18, the dams were euthanized and their fetuses were weighed and examined for abnormalities. The results were anomalous: only the number of litters with abnormalities exposed at the lowest power density (3.4 W/kg) significantly differed from the sham exposed group. However, the mean live fetal weights of those exposed at 28 mW/cm² were also significantly lower.

Berman et al. [1982] also exposed time-bred CD-1 mice to the same RFEMF frequency, level, and duration, but on gestation days 6 through 17, and euthanized the dams on day 18. The numbers of live, dead, and resorbed fetuses and total number of live fetuses in the RFEMF mice were comparable to those in the sham exposed mice, but the mean body weight of the exposed live fetuses was significantly smaller than for the sham exposed fetuses. In addition, for dams allowed to come to term, the mean body weight at age 7 days of the exposed pups was significantly smaller than for the sham exposed pups. Berman et al. [1984] confirmed those significant differences, but in addition, found that brain weights at ages 10, 12, and 17 days were consistently lower for the exposed neonates than for the sham exposed pups. The authors indicated that the whole body SAR in this study, 16.5 W/kg, may have heat stressed the mice, thereby causing the brain weight deficit.

Nawrot et al. [1981] exposed pregnant CD-1 mice to 2.45 GHz RFEMF daily for 8 h on various gestation days at incident power densities of 5, 21, or 30 mW/cm². Other groups were heated conventionally at 30 or 31 °C, respectively, to obtain the same rises in colonic temperature as with the two higher RFEMF levels. Two groups of mice were given each treatment, one characterized as “handled” and the other as “nonhandled.” In the first experiment, groups were exposed on gestation days 1–15 at 5 mW/cm² (6.7 W/kg). In the second experiment, groups were exposed at 21 mW/cm² (28.1 W/kg) or to 30 °C ambient temperature, both of which induced a rectal temperature rise of about 1 °C. All groups were treated daily on gestation days 1–6. A third experiment was similar to the second, but with treatment at 30 mW/cm² (40.2 W/kg) or ambient heating at 31 °C to obtain a temperature rise of 2.3 °C. Significant effects (lower fetal weight, lower dam weight gain, fetal malformations) were ascribed by the authors to interaction between exposure and handling. They concluded that the threshold for teratogenic effects is about 30 mW/cm² (whole body SAR of 40.2 W/kg). Nawrot et al. [1985] subsequently obtained similar findings of an interaction between exposure and handling.

Inouye et al. [1982b] exposed mated female CD-1 mice to 2.45 GHz RFEMF on day 2 (2 cell embryonic stage) and day 3 (4 cell to 8 cell stage) at 9 or 19 mW/cm². Other mice were heated at ambient 38 °C. No rise in colonic temperature was seen with 9 mW/cm², a 1 °C rise occurred at 19 mW/cm², and at least a 2.2 °C increase occurred for the 38 °C heat treatment. The dams were euthanized on day 4, and the embryos were counted and examined for abnormalities. No significant differences were found in embryonic...
development or abnormal embryos between the RFEMF and sham groups, but the 38 °C heat treatment had stunted embryonic development.

**Rats**

Dietzel [1975] exposed pregnant rats once each on a single day during gestation days 1–16 to 27.12 MHz RFEMF at 55, 70, or 100 W for up to 10 min. Each rat was removed from the field when its temperature reached 39, 40.5, or 42 °C. On day 20, the fetuses were counted, weighed, and examined for external malformations. Typical predominant abnormalities were neurocranial malformations from exposure on day 9 or 10, kinked or short tails and “hand” defects for day 13 or 14, and cleft palate for day 15. The largest numbers of abnormalities occurred for exposure on days 13 and 14 and correlated well with rectal temperature increases.

Chernovetz et al. [1977] exposed pregnant rats for 20 min on only 1 day during gestation days 10–17 to 2.45 GHz RFEMF at 31 W/kg mean SAR. Other rats were either sham exposed or exposed to infrared radiation (IR) to obtain the 3.5 °C colonic temperature rise seen for RFEMF exposure. On day 19, the dams were euthanized, the numbers of implantations and resorptions were counted, and fetuses were weighed and examined for abnormalities. Mean fetal mass for the IR and RFEMF groups were both significantly lower than for the sham group. The authors concluded that the effects observed were the result of the increased maternal temperatures.

Smialowicz et al. [1979] exposed pregnant rats to 2.45 GHz RFEMF at 5 mW/cm² for 4 h per day, 7 days a week, from gestation day 6 through term. Following birth, a group of male pups from each dam were similarly treated until age 20 days, at which time half were euthanized and the other half were treated until age 40 days and then euthanized. Both the dams and pups were weighed at selected intervals. There were no significant differences in mean weight between the RFEMF and sham exposed animals.

Berman et al. [1981] exposed pregnant CD rats to 2.45 GHz RFEMF at 28 mW/cm² (SAR: 4.2 W/kg) daily for 100 min on gestation days 6 through 15. The mean colonic temperature at the end of each exposure period was 40.3 °C. On gestation day 21, each rat was euthanized and the live, dead, and resorbed conceptuses were counted. Live fetuses were examined for external and internal morphology, and weighed. There were no significant differences between RFEMF and sham exposed groups in any endpoint. In a similar study, Berman and Carter [1984] exposed 24 pregnant Sprague–Dawley rats at 40 mW/cm² (SAR: 6 W/kg) for 100 min daily on days 6 through 15. On day 21, the uteri were examined for pregnancy and numbers of live, dead, and resorptions. On a per litter basis, no significant differences were seen between groups in the latter endpoints. The only significant differences were lower mean fetal weight and the number of ossified sternebrae in the RFEMF group.

A number of teratologic studies were performed with the 27.12 MHz ISM band used in the heat-sealing industry [Lary et al., 1982, 1983a,b, 1986; Tofani et al., 1986; Brown-Woodman et al., 1988]. Lary et al. [1982] exposed pregnant Sprague–Dawley rats on gestation days 1, 3, 5, 7, 9, 11, 13 in a near field synthesizer in which the free space-equivalent power density was about 138 mW/cm² (SAR about 12 W/kg), conditions selected to deliver doses nearly hyperthermically lethal to the dams. The exposures were terminated when colonic temperature reached 43 °C (duration 20–40 min). The dams were euthanized on day 20 and the implantations, live and dead fetuses, and resorptions were counted. Each live fetus was examined for various abnormalities, measured for crown-rump length, and weighed. More than 200 different types of abnormalities were seen in the RFEMF exposed group, most of which occurred for exposure on gestation day 9, and many of which were severe malformations.

Lary et al. [1983a] treated pregnant rats to several high level exposures to 27.12 MHz only on gestation day 9. The percentage of malformations and the ratio of litters affected increased with increasing exposure level, with the largest change at prolonged 42.0 °C colonic temperature. The authors ascribed those effects to the hyperthermia induced by the RFEMF.

Lary et al. [1983b] exposed pregnant rats to 100 MHz RFEMF within a transverse electromagnetic (TEM) cell at 25 mW/cm² for more than 6 h per day on gestation days 6–11. The mean whole body SAR was about 0.4 W/kg. As controls, 32 pregnant rats were sham exposed in a mock TEM cell. The rats were examined postexposure for numbers of implantations, live and dead fetuses, and resorptions, and the fetuses were weighed, measured for crown-rump length, and examined for gross abnormalities. There were no significant differences between the groups in any of those endpoints. Surprisingly, the RFEMF exposed group had fewer minor skeletal variations than the sham exposed group. Thus, the results yielded no evidence that exposure at 0.4 W/kg was embryotoxic or teratogenic.

Lary et al. [1986] also investigated the dose–response relationship between RFEMF induced maternal increases in body temperature and incidence of birth defects in rats. They exposed pregnant rats on gestation day 9 to 27.12 MHz RFEMF at 10.8 W/kg whole body SAR. The exposures were terminated when colonic temperatures reached 41, 41.5, 42, 42.5, or 43.0 °C. The dams were euthanized on day 20 and counts of the
various types of fetal abnormalities and deaths were plotted versus colonic temperature. The results indicated a temperature threshold of 41.5 °C for teratologic effects.

Tofani et al. [1986] exposed pregnant rats continuously to 27.12 MHz RFEMF at field strengths of 20 V/m and 0.05 A/m during gestation days 0–20, 0–6, or 6–15. The authors estimated the SAR at these field strengths to be about 0.00011 W/kg. Resorptions were statistically significant for the two groups exposed from day 0 of gestation, suggesting that this effect occurred during the early stage of egg development. Mean litter weights of the exposed groups were significantly lower than the sham group, as well as greater incidence of incomplete ossification of cranial bones. The authors regarded the reported effects as nonthermal and due to long term exposure. Lu and Michaelson [1987] questioned the validity of this study, citing the lack of technical details and other experimental deficiencies.

Brown-Woodman et al. [1988] investigated whether teratogenesis induced in rats by 27.12 MHz CW RFEMF is due to hyperthermia. They exposed pregnant Sprague–Dawley rats on gestation 9 with a diathermy unit. The amplitudes of the electric and magnetic fields were 33 kV/m and 0.8 A/m, and the estimated whole body SAR was 11.2 W/kg. The exposures were for durations needed to reach specific core temperature increases, at which points, 1 min bursts of the RFEMF were used maintain that rise for an appropriate period. Control rats were sham exposed. Core temperatures of other rats were raised for specified durations by nonRFEMF heating with 2.5–5.0 °C in 0.5 °C steps.

The dams were euthanized on day 20; their uterine horns were examined for the number of implantations; and both live and dead fetuses were counted, weighed, and examined for gross malformations. There were no significant differences in mean embryo weight irrespective of RFEMF exposure level. However, the results for heating the rats by nonRFEMF means were as follows: a 5.0 °C rise for a few seconds raised the resorption rate to 74%. The body weights of surviving fetuses were significantly reduced, and all exhibited a variety malformations. Elevations by 4.5 °C for 2, 5, or 10 min yielded lethality increases and higher numbers of abnormal litters with increasing duration, with microphthalmia as the most common malformation. Temperature rises of 4.0 °C for 3, 5, 10, or 15 °C caused similar duration dependent results. However, no teratologic effects were seen with rises of 3.5 °C for 10 or 15 min, but longer durations yielded increases in lethality and number of abnormal fetuses. Progressive reductions in deleterious effects were seen for elevations by 3.0 and 2.5 °C.

The authors concluded that the teratogenic and embryolethal effects they observed were related primarily to both core temperature elevation and its duration, with a threshold core temperature rise of about 2.5 °C.

Inouye et al. [1983] exposed pregnant Sprague–Dawley rats to 2.45 GHz RFEMF at 10 mW/cm² for 3 h daily on gestation days 4 through 21 (SAR about 2 W/kg) and allowed them to come to term. Two day old neonates were separated from their dams and fostered to unexposed dams. From age 2 days through 40 days, those neonates were weighed daily and exposed at 10 mW/cm² for 3 h. Plots of mean body weights versus age showed no differences between the exposed and sham exposed rats.

At ages 15, 20, 30, and 40 days, groups of six pups each were euthanized and fixed by perfusion. The brains were removed, weighed, measured, and given neuroanatomical examination. At corresponding ages, no significant differences were found between exposed and sham exposed pups in brain weights, cerebral dimensions, or histologic parameters. In the 40 day old pups, there were no significant differences between the exposed and sham exposed pups in dendritic spine densities, nor were there differences in counts of Purkinje cells between the groups. The authors remarked that this result was contrary to the finding by Albert et al. [1981] of fewer Purkinje cells in exposed rats.

Jensh et al. [1982] exposed pregnant Wistar albino rats to 915 MHz RFEMF at 10 mW/cm² (SAR ~4 W/kg) for 6 h per day on gestation days 1–21 and euthanized them on day 22. No statistically significant differences were found in mean litter size or mean fetal weights between exposed and sham exposed rats. These negative findings are consonant with those of Chernovetz et al. [1977] and Berman et al. [1981] at 2.45 GHz, and of Lary et al. [1982, 1983] and Brown-Woodman et al. [1988] at 27.12 MHz, which indicated that exposure to much higher SARs are necessary for teratologic effects in rats.

Jensh et al. [1983a,b] described the first of several paired teratogenesis studies. In Jensh et al. [1983a], pregnant rats were exposed 6 h daily throughout gestation to 2.45 GHz RFEMF at 20 mW/cm² and were euthanized on day 22. The estimated mean SARs during gestation periods 0–1, 7–8, and 20 days, respectively, were 5.2, 4.8, and 3.6 W/kg. No significant differences between exposed and sham groups were found in fetal weight, resorption rate, or abnormalities. The authors concluded that protracted exposure of dams throughout gestation to this frequency and level was not embryotoxic. In Jensh et al. [1983b], pregnant rats were similarly treated but allowed to come to term. Growth rates of the neonates from exposed and sham groups during corresponding periods up to 87 days of age did
not differ significantly. Linear regression analysis of those data also indicated nonsignificance.

In a similar study using 6 GHz RFEMF at 35 mW/cm², Jensch [1984a] exposed pregnant rats for 6 h/day throughout gestation, euthanized them on gestation day 22, and investigated similar endpoints. Again, no significant differences were seen except for lower mean fetal weight at term for the RFEMF exposed rats. The authors suggested that this growth retardation could be “a manifestation of a generalized compensated heat stress reaction.” They concluded that exposure to 6 GHz RFEMF at 35 mW/cm² is not overtly teratogenic.

In Jensch [1984b], F1a offspring at age 90 days were bled within and across groups, and teratologic evaluations were done on 659 F2 (second generation) term fetuses. The original dams were reared 10 days after weaning the F1a pups, and teratologic evaluations were completed on 263 F1b offspring. Organ weight analyses were done on some original dams and F1a adult offspring.

The mean maternal weight of RFEMF dams on day 21 of first breeding was smaller than for controls, as was the mean litter size. A few F1a pups in both groups exhibited cataracts, but no other abnormalities were evident. Breeding exposed adult female F1a rats with exposed adult males and cross-breeding exposed rats with control rats yielded smaller mean maternal weight increases during gestation. The mean organ-to-body weight ratios of RFEMF exposed and sham exposed adult F1a males differed significantly only for the left kidney and the right testis, with the mean values larger for the RFEMF group. For the RFEMF exposed and sham exposed females, the only significant ratio difference was for the liver.

About the F2 offspring, the author stated: “Mean litter sizes differed significantly only between the irradiated female × irradiated male and the sham female × sham male groups (P < .05). Both the litter size and the resorption rate varied inversely with the exposure groups . . . .”

Perhaps the most important finding of this study was absence of any terata in F1a, F1b, and F2 offspring from prolonged exposure (8 h/day) to 6 GHz RFEMF at 35 mW/cm² (SAR about 7 W/kg). This finding is consonant with those of Berman et al. [1981].

Merritt et al. [1984] exposed ten pregnant Sprague–Dawley rats, starting on gestation day 2, to circularly polarized pulsed 2.45 GHz RFEMF in individual cylindrical waveguides. The exposures were for 24 h/day, 7 days/week, until day 18. The SARs for the dams were held constant at 0.4 W/kg as their weights increased with time. The dams were euthanized every fourth day. On day 18, they were euthanized and their fetuses were removed. The body and brain of each dam were weighed and its brain was homogenized and assayed for RNA, DNA, and protein. The latter three endpoints were reported in terms of both mg/brain and µg/mg of brain tissue, totaling eight endpoints. The difference between the groups for each endpoint was nonsignificant.

The effects of the chronic RFEMF exposure on brain development were assessed from a linear regression plot of mean litter brain weight on mean litter body weight for the sham group. The mean values for the RFEMF group, plotted on the same graph, were found to be scattered about the regression line. The criterion used to indicate whether litters were microencephalous was a regression line two standard errors (SEs) below the regression line for the sham group. All of the mean values for the exposed group were above that criterion line, thus indicating that no exposed litter was microencephalous.

Schmidt et al. [1984] chronically exposed pregnant Sprague–Dawley rats during gestation days 2–18 in a circular waveguide exposure system. The rats were weighed periodically, and the input power to the waveguides was adjusted for the weight increases with age to maintain a constant SAR of 0.4 W/kg. The dams were euthanized on day 18, the uterus of each was excised, and its implantation sites were counted. Each uterus was then immersed in physiological saline, and individual implantation sites were opened. The fetuses were tested for viability and weighed, their crown-rump lengths were measured, and they were examined for gross external malformations.

Fetuses of one group were fixed, sectioned, stained, and examined by light microscopy for internal organ malformations or possible embryotoxic lesions. Those of another group were cleared, stained, and examined for skeletal abnormalities with a microscope. There were no differences between the exposed and sham exposed groups with regard to any of the examined endpoints. The authors concluded that essentially continuous exposure of pregnant rats during gestation days 2–18 to 2.45 GHz RFEMF at 0.4 W/kg is neither teratogenic nor embryotoxic.

Klug et al. [1997] investigated whether interactions of amplitude modulated electric or magnetic fields with living systems could produce teratologic effects at nonthermal levels, using a 150 MHz rectangular cavity resonator that provided spatial separation of the maxima of the two fields. The respective field strengths were 60 or 600 V/m and 0.2 or 2.0 µT, 100% amplitude modulated at 16, 60, or 120 Hz. The authors also exposed embryos to 900 MHz RFEMF modulated at 217 Hz, said to simulate conditions for digital mobile telecommunication. The embryos were very small, so
the fields were measured with minute electric dipolar and magnetic induction loop probes to avoid perturbations. In addition, to ensure transfer of probe data without interfering with the standing wave fields, those data were converted into ultrasound and conveyed outward by quartz rods.

In one 150 MHz experimental set, 9.5 day old Wistar rat embryos (2–3 somites) were cultured in a specified medium for 48 h at 38.5 °C, and three or four embryos per culture vessel were exposed in vitro to the electric or magnetic field during the first 36 h of the culture period. Then the embryos were incubated under control conditions for the remainder of the 48 h period. At that time, serial sections of the embryos were assessed for growth (crown-rump length, protein content) and differentiation (development of somites) by light and electron microscopy. Also assessed were the percentages of dysmorphogenic embryos. No significant differences in any of the endpoints relative to sham exposed cultures were found, except for a decrease in numbers of somites for the embryos exposed to the 16 Hz modulated electric field at 600 A/m. However, the authors noted that up to 10% of differences in somite numbers and dysmorphogenic embryos are in the range of historic controls in this culture system, and they therefore, did not consider the results as indicative of an effect of the exposure regimen.

In another set of experiments, they exposed embryos to peak amplitudes of 0, 14, 32, and 71 V/m. The corresponding SARs were 0, 0.2, 1.0, and 5.0 W/kg. At 0.2 W/kg, the only significant differences were in median somite numbers and protein content for 12 field exposed dysmorphogenic embryos versus 4 in the control group. At 1.0 W/kg, only seven dysmorphogenic embryos were found, and the differences for the other endpoints were not significant. Also, no dysmorphogenic embryos were found at 5.0 W/kg.

In view of the negative findings above and the expected 10% numbers of somites and dysmorphogenic embryos in controls, the authors concluded that neither the electric nor the magnetic fields had significant effects on the growth and differentiation of the cultured embryos. Similar negative findings were also reported for embryos exposed to 900 MHz RFEMF modulated at 217 Hz.

Bornhausen and Scheingraber [2000] investigated whether exposure of pregnant Wistar rats to 900 MHz RFEMF at 0.1 mW/cm², the maximum level permitted for European GSM base stations, would alter the behavior of their offspring. Using a dish antenna at the top of the exposure chamber, the authors continuously exposed a group of 12 first-time pregnant rats to 0.577 ms pulses of circularly polarized 900 MHz RFEMF at a rate of 217 pps during gestation days 1–20. Another group was concurrently sham exposed in a similar chamber. Whole body SARs were measured in rat models, each consisting of a single rat among other freely roaming rats within the chamber in each experiment. The SARs ranged between 17.9 and 75 mW/kg, depending on the specific configurations of the roaming subgroups of rats. At parturition, four male and four females were selected from each dam, using the criterion that the total weight of those eight pups be about the same as the mean weight for that litter. At weaning age (21 days), the pups were coded.

At age 3 months, the behaviors of the rats were tested concurrently during 15 h night sessions in a set of ten simultaneously operated automated chambers (Skinner boxes). The food reinforced lever pressing activities and inter-response intervals (IRIs) between lever presses were measured to determine differential reinforcement of high (DRH) or reinforcement of low (DRL) responses. Also, consecutive IRIs were correlated with specific test requirements of the DRH or DRL sessions. Each chamber contained two levers with three cue lights above each lever, a house light, and receptacles for food and water.

Each test group consisted of five exposed and five sham exposed rats. The rats were not food-deprived, shaped, or habituated before their training sessions, which were designed to achieve criterion performance as described in detail in the paper. After training, the rats were required to respond at high (DRH) or low (DRL) rates, to distinguish between cognitive and motor response deficits, exemplified by the authors as follows: In a DRH 4/2 test, the rat must press the correct lever four times within 2 s, whereas in a DRL 1/16 test, it must respect a blocking interval of 16 s (duration signaled by a cue) between two lever presses. The actual tests consisted of three different schedules of increasing learning demand, with each schedule comprising various combinations of the foregoing. The data were analyzed by the Mann–Whitney U-test or the Wilcoxon Rank-Sum test.

The authors found no significant differences between RFEMF exposed and sham exposed dams or offspring in litter size, increase in body mass with age, developmental differences with litter mates, or learning ability during training. The performance results were presented in the paper’s Figure 1 as bar graphs of percentage performance efficiency and SDs for the various operant schedules. For each schedule, there were no significant differences between RFEMF exposed and sham exposed groups or between males and females. Performances normalized to those for sham exposure were shown in the paper’s Figure 2 for specific schedules. The data were widely scattered but roughly symmetrical about the 1.0 line. Of particular interest
was the ability of distinguishing between “learners” and “nonlearners,” exemplified in the author’s Figure 5.

Open to question was the concurrent exposure of groups of free roaming rats because of likely uncontrolled field interactions among the animals in each group and differences among exposure groups. In addition, the use of rat models among such roaming groups, which presumably led to the large spread of whole body SARs, obscures the relationship (if any) of the negative findings to the RFEMF dose rate and the large SDs in Figure 1.

**NONHUMAN PRIMATES**

Kaplan et al. [1982] had exposed 33 squirrel monkeys during the second trimester of pregnancy for 3 h/day, 5 days/week until parturition to 2.45 GHz RFEMF at whole body SARs of 0.034, 0.34, or 3.4 W/kg (low, intermediate, or high level) in multimode, mode stirred microwave cavities [Heynick et al., 1977]. The primary objective was to determine whether such chronic exposure would alter mother–offspring behavioral patterns and the EEG. Other behavioral endpoints included perceptual and motor capabilities, the results of which are summarized later.

Eight pregnant monkeys were similarly sham exposed. After parturition, 18 of the RFEMF exposed dams and their offspring were exposed to the RFEMF for 6 more months; then the offspring were exposed without the dams for another 6 months.

Live births occurred for 30 of the 33 RFEMF exposed dams and for all eight sham exposed dams. Regarding the other three dams, the neonates for two of them exposed at the high level and one dam exposed at the intermediate level died within a day or two after parturition. These three dams comprised only 10% of the total exposed, but similar deaths had not occurred in more than 250 pregnancies during the 5 previous years of the colony.

The live offspring were weighed weekly for the first 8 weeks of age and monthly thereafter until they were 1 year old. There were no significant weight differences between the groups at corresponding ages. Of the infants exposed only prenatally and born alive, two of the four exposed at the low level died (at ages 32 and 83 days), none of the six exposed at the intermediate level died, and one of the four exposed at the high level died (at age 4 days). Regarding the results for the 16 exposed both prenatally and postnatally, none of the five exposed at the low level died, two of the six exposed at the intermediate level died (at ages 38 and 49 days), and four of the five exposed at the high level died (at ages 58, 78, 143, and 177 days). However, the annual mortality rate during the first year of life for the

In all but one case, the infant deaths occurred without warning; each was found in its home cage in the morning. Necropsies had not been planned, were not performed on any of the adults because of autolysis, and were performed on only four of the nine dead offspring. In none of these cases could the cause of death be determined.

However, as stated in a note added in proof to Kaplan et al. [1982], a followup study was performed at only 3.4 W/kg with infant mortality as the major endpoint and with a sufficient numbers of animals for greater statistical validity. Although no data were included in the note, the authors stated that no statistically significant differences in infant mortality were found between the RFEMF and control groups, thus vitiating the earlier mortality findings.

In the original study, among the other endpoints tested in infants were righting, orienting, climbing down, climbing up, and directed locomotion. The authors noted that because of the large variability within all groups and small group sizes, they scored their results and analyzed them with the nonparametric Kruskal–Wallis analysis of variance by ranks. On that basis, there were no significant differences among the findings in these endpoints for the three RFEMF levels and sham exposure.

Baseline EEGs and changes thereof following prenatal RFEMF exposure of the dams, postnatal exposure of mothers and offspring at weaning time (infant age 6 months), and at ages 9 and 12 months were performed by stimulation with light flashes in blocks of 20 trials at 6, 10, and 16 flashes per second. Again, Kruskal–Wallis analysis showed no significant differences among groups, irrespective of whether the RFEMF exposures were prenatal, postnatal, or both.

**EPIDEMIOLOGIC STUDIES**

It is important to note that positive or negative findings reported in epidemiologic studies should not be regarded as firm scientific evidence, useful for standards setting, because of the absence of adequately quantified dosimetric data, use of possibly inaccurate responses to questionnaires, and other similar problems.
likely to lead to questionable findings. However, such studies can be useful as indicators of possible topics for future experimental research, an aspect beyond the scope of this paper, which deals only with already published findings. Nevertheless, this epidemiologic section does provide most of the data on real or assumed human RFEMF exposures, both in occupational settings and members of the general public.

In an early epidemiologic study, Sigler et al. [1965] discussed a possible relationship between the occurrence of Down’s syndrome (“mongolism”) and presumed exposure of the fathers to RFEMF from radars during military service. The authors examined data, derived from Baltimore hospital records and interviews with parents, on 216 Caucasian children with Down’s syndrome. The case children were matched with 216 control children. The major significant finding was that the percentage of case mothers exposed to ionizing radiation was higher than for the control mothers. Also discussed, however, was a possible association between Down’s syndrome incidence and paternal radar exposure.

Cohen et al. [1977] reexamined the Sigler et al. data, along with the data on 128 additional matched pairs. The results did not confirm any link between paternal RFEMF exposure and Down’s syndrome in their progeny.

Peacock et al. [1971] sought to assess whether the incidence of birth defects in Alabama could be associated with proximity to military bases. They examined a statewide file of birth certificates by counties and found that the anomalies per 1000 for births to military families was much higher than the anomaly rate for civilian births in the six county area surrounding Fort Rucker. Peacock et al. [1973] subsequently reassessed that premise with additional data by comparing fetal anomaly rates in the military hospitals at Fort Rucker and Eglin Air Force Base (“radar bases”) with those of three military hospitals at bases that had “minimal” radar networks. They confirmed that the anomaly rates for several specific anomalies and numbers of fetal deaths were abnormally high at Fort Rucker’s Lyster Hospital and that the numbers of fetal deaths in the hospital at Eglin Air Force Base were comparable.

Burdeshaw and Schaffer [1977] compared the data for the two counties in which Fort Rucker is located with data from the other counties in Alabama. The greater incidence of congenital anomalies at Lyster Hospital was found to be attributable to a higher than normal reporting rate by one physician, who apparently had included “birth defects” not considered as such by other physicians. Also, the major defect in Peacock et al. [1971, 1973] was the absence of assessment of the putative exposure of the mothers.

Källén et al. [1982] hypothesized that Swedish physiotherapists were likely to have been exposed occupationally more than the general population to various agents, including RFEMF. They performed a cohort study on infants born during years 1973–1978 to women registered as physiotherapists during their pregnancies. They analyzed this cohort for perinatal mortality and the occurrence of malformations by comparing those data with information on all births in the Swedish Medical Birth Register. The results showed that for all endpoints, the expectation values for the total cohort were statistically better than or comparable to those for the general population.

The authors then hypothesized that if hazardous exposure had occurred, it should be more common among the few females who had dead or malformed infants than among those who had normal babies. They, therefore, did a case-control study within the cohort, in which 37 infants were selected who had major malformations or had died perinatally, and compared them with two normal infants for each case. The exposures for case and control mothers were estimated from answers to a questionnaire. The authors found that the physiotherapists as a group had a slightly better outcome than in the general Swedish population, but reported that use of shortwave equipment was higher among physiotherapists who had given birth to a malformed or perinatally dead infant. Statistically, however, those results would change from borderline significance to nonsignificance if one or two answers to the questionnaire were based on faulty recall by the respondents.

Taskinen et al. [1990] did a study of all registered physiotherapists in Finland who had become pregnant during 1973–1983, to determine whether occupational exposure to various patient treatment modalities, including RFEMF, is associated with spontaneous abortion or congenital malformations in their offspring. Their data were also obtained from the responses to questionnaires. From multivariate analyses, the odds ratio (OR) for spontaneous abortions was significant for physiotherapists using shortwave and microwave diathermy devices 5 or more h/week, but not for use 1–4 h/week. By contrast, a significant increase in risk of congenital malformations was reported from administering shortwave diathermy therapy for 1–4 h/week, but not for 5 or more h/week.

The authors remarked: “The results of this study suggest that heavy physical exertion is a risk factor for spontaneous abortion. The effect of shortwaves and ultrasound on ‘late’ spontaneous abortions was significant and increased in a dose related manner. On the other hand, in the multivariate analyses neither the effects of ultrasound nor shortwaves reached statistical
significance. Therefore, the finding has to be interpreted cautiously. The finding of an association between the exposure to shortwaves and congenital malformations does not justify conclusions of a causal relationship.”

Larsen [1991] assessed whether occupational exposure of Danish physiotherapists to high frequency electromagnetic fields increases incidence of congenital malformations. The cases and referents were identified by links with national registers. The RFEMF exposure levels were estimated by telephone interviews with the respondents, using a scale of 0–1 based on the time spent per week in the room where RFEMF was used. The OR for congenital malformations versus exposure duration was not significant. Overall, this study provided no statistically valid evidence that exposure of physiotherapists to shortwaves is a cause for birth of malformed infants.

Larsen et al. [1991] interviewed by phone almost all of the physiotherapists in Denmark about RFEMF exposure during their pregnancies. The information gathered concerned all spontaneous abortions treated in hospitals and deliveries during that period. It also included data on induced abortions, gestation durations, number of births, birth weights, gender, perinatal deaths, birthplaces, and mothers’ ages. A time-weighted exposure index was divided into three categories: 0 for no exposure, 1 for low exposure, and 2 for high exposure. The results for spontaneous abortions, subfecundity, stillbirth, or death within 1 year, premature birth, and low birth weight showed no significant differences. The major positive finding was a low ratio of boys to girls born to the physiotherapists exposed to shortwaves, an unexpected result.

Little credence can be given these occupational studies of physiotherapists, mostly because of the essentially qualitative exposure estimates used. Moreover, Gubéran et al. [1994] were unable to confirm the low male/female gender ratios reported by Larsen et al. [1991].

Ouellet-Hellstrom and Stewart [1993] mailed questionnaires to 42403 female physical therapists to assess possible effects on them from occupational use of microwave and shortwave diathermy, specifically an excess risk of miscarriage. Case and control therapists who had not worked during the 6 months prior to and during the first pregnancy trimester were classified as unexposed. Groups were taken as exposed if they had been working and had reported using microwave or shortwave diathermy during that time interval. The authors reported that the pregnancies of mothers who used microwave therapy modalities during those periods were more likely to result in miscarriages. For this group, the OR was 1.26 with a 95% confidence interval (CI) of 1.02–1.59 (barely significant). In addition, the OR increased with increasing levels of exposure. Thus, these authors linked such miscarriages only to microwave therapy.

More recently, Lerman et al. [2001] assessed whether the following adverse pregnancy outcomes of physiotherapists in Israel were linked with RFEMF exposure: spontaneous abortions, congenital malformations, premature birth, and low birth weight. They sent an anonymous questionnaire to all members of the Union of Israeli Physiotherapists. The resulting case population comprised 175 physiotherapists who had reported spontaneous abortions before gestation day 28, 45 of who had infants with congenital malformations, 47 with premature delivery (before gestation week 36), and 33 with low infant birth weight. The controls were 633 mothers who had reported no adverse pregnancies. The OR for congenital malformations was 2.24 with a CI of 1.27–4.83, $P = .006$ (statistically significant). The data on low birth weight and shortwave exposure yielded an OR of 2.99 with a CI of 1.32–6.79 (also significant). However, the authors stated that after controlling for possible confounding variables, the data for congenital malformations ascribed to RFEMF exposure were not statistically significant, whereas those for low birth weight were, suggesting that exposure to shortwaves could be potentially harmful to pregnancy outcome.

**OVERALL CONCLUSIONS**

Most of the investigations on teratogenesis, including prenatal and postnatal lethality, were done with RFEMF levels well in excess of the IEEE [1999] maximum permissible exposure guidelines and with relatively crude dosimetry. One of several early studies of darkling beetle pupae indicated a possible non-thermal effect, but another study with more precise dosimetry showed that nonRFEMF confounding factors were likely present. Many studies were done with rodents at levels that caused elevated body temperatures. An interesting experimental finding was that although mice exhibited various teratologic effects at such levels, the primary findings in rats were lower birthweights and slower growth rates. A behavioral study of pregnant squirrel monkeys exposed to 2.45 GHz RFEMF at up to 3.4 W/kg and of their infants, directed toward possible effects on dam and infant interactions and EEGs, yielded negative findings. However, a number of unexplained infant deaths had occurred, and a follow-up study with infant death as the sole endpoint, using a larger number of dams for greater statistical validity, did not confirm that finding.

In conclusion regarding experimental studies with nonhuman species, teratogenic effects can occur in both
nonmammalian and mammalian subjects from RFEMF exposure, but only at levels that produce significant internal temperature rises. Such positive findings were consonant with those of experiments with various nonRFEMF heating modes. For mammals, maternal body temperature rises that exceed specific thresholds, for each species, are necessary for causing such effects. Those thresholds are far above the maximum exposure levels specified in the IEEE [1999] guidelines. No credible experimental evidence was found for nonthermal RFEMF teratologic effects.

Mixed or contradictory findings were reported in several epidemiologic studies on congenital anomalies due to presumed public exposure to RFEMF from nearby sources. However, critical analyses of those studies indicate that none of them provide valid evidence that chronic exposure of mothers during pregnancy or of potential fathers to RFEMF at levels at or below IEEE [1999] maximum permissible exposure guidelines would cause adverse pregnancy outcomes or any anomalies in their offspring. Moreover, epidemiologic studies of the pregnant physiotherapists occupationally exposed to several forms of RFEMF used for treating patients yielded mixed teratologic findings on their fetuses and postpartum outcomes. Taken collectively, however, the findings do not support the premise of adverse RFEMF effects on pregnancy outcome.

In overall conclusion, excessive temperature elevations, whether from RFEMF exposure or more conventional heating are teratogenic, and no valid experimental evidence was found for the occurrence of nonthermal teratogenic effects.

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REFERENCES


