comparable to that of the geomagnetic field. Theoretically frequencies up to 1 kHz or higher, depending on the ion involved, can be effective under these conditions. It is proposed that the frequency of interaction is related to the ion characteristics and the static magnetic flux density according to the following relationship:

$$f = kBq/m \qquad \text{(Equation 6.6)}$$

where: f is the resonant frequency, k is a constant (integer), q is the ion charge, m is the ion mass, and B is the constant magnetic flux density. Some of the earlier models, such as the cyclotron resonance (Liboff, 1985; McLeod & Liboff, 1986), suffered from serious limitations (Halle 1988). Other models appear worthy of closer scrutiny (Lednev, 1990; Male & Edwards, 1990).

Overall, the experimental data for q/m effects on ion binding to the membrane or enzyme surfaces and on cation transport through cell membrane pores are intriguing, but there is a clear need for refinements in the theoretical description of this phenomenon and to substantiate the experimental results. Whether, and how, any of the resonance models (Chiabrera et al., 1984; Liboff, 1985; McLeod & Liboff, 1986; Lednev, 1990; Male & Edmonds, 1990) can be applied to RF fields amplitude modulated at ELF has not yet been considered or tested.

6.4.4 Calcium ion exchange

An observed change in the EEG pattern of cats exposed to 147 MHz fields amplitude modulated at ELF, prompted further investigation with an isolated chick-brain tissue preparation, to determine whether the presence of the peripheral nervous system was required to elicit a change in the central nervous system. Statistically significant increases in labelled calcium ion efflux were observed in isolated tissues exposed to 10-20 W/m^2, 147 MHz fields amplitude-modulated at frequencies from 6-20 Hz, but levels remained the same as control levels at modulation frequencies of less than 6 Hz or greater than 20 Hz. No effect on calcium ion efflux was observed from exposure to unmodulated RF fields (Bawin et al., 1975). The SAR was less than 0.004 W/kg. This field-induced effect is of interest because it occurs at SARs too low to implicate heating, and because calcium ions play a prominent role in the transductive coupling of many cell membrane-mediated responses. Thus, this *in*

vitro result provides a means of interrogating the function and processes occurring at the cell membrane and of identifying possible subtle mechanisms of interaction of RF fields.

Using 50, 147, and 450 MHz carrier waves, this work has been replicated and extended with one or more modulation frequency or power density windows being reported (Blackman et al., 1979, 1980a,b, 1985, 1989; Sheppard et al., 1979). A power density window centred on 8.3 W/m^2 (0.0014 W/kg) has been reported. Six power density windows were observed for 16 Hz modulated 50 MHz, with five of the windows separated by a geometric relationship that may reveal a characteristic of the underlying mechanism (Blackman 1980a,b, 1985, 1989).

Lee et al. (1987) reported enhanced release of calcium ions from chick-brain tissue exposed in two power density regions of 147 MHz fields, modulated at 16 Hz, only when specific temperature conditions were instituted in the preparation of the tissue. The temperature conditions during sample preparation were also shown to affect the relative direction of the efflux and to control the sensitivity of the brain tissue samples to ELF signals (Blackman et al., 1991). The release of calcium ions from a rat synaptosomal preparation was also reported to be affected by 450 MHz, amplitude modulated at 16 Hz, at 10 W/m^2 (Lin-Liu & Adey, 1982).

Exposures at 315 Hz and at 405 Hz, at intensities of 15 V/m and 60 nT, were reported to enhance calcium efflux, whereas intensities between, above, and immediately below these values did not (Blackman et al., 1988). The 315 Hz exposure was dependent on the perpendicular flux density and orientation of the DC magnetic field of the earth (Blackman et al., 1990). Additional work at lower frequencies suggests that the DC magnetic field may have a direct influence on which frequencies are effective (Blackman et al., 1985).

Some investigators have reported null results with brain tissue preparations. Shelton & Merritt (1981) did not observe any changes in the release of calcium ions from an *in vitro* rat brain tissue preparation exposed to 1 GHz, pulse modulated at 16 or 32 Hz, at 5, 10, 20, or 150 W/m^2. Similarly, no effects were observed with rat tissue labelled *in vivo* and exposed *in vitro* or *in vivo* to 1 GHz or 2.06 GHz, pulse modulated at several ELF and power density combinations (Merritt et al., 1982). Null effects were also reported

by Albert et al. (1987) using chick brain tissue exposed to a few power densities of 147 MHz, amplitude modulated at 16 Hz, under anoxic and under modified media conditions designed to supply more oxygen to the tissue.

In none of these null-effect experiments did the authors reproduce the exposure conditions used by Bawin or Blackman, particularly the medium composition, power density, sinusoidal modulation, or number of samples per experiment.

Increases in calcium ion efflux have been reported in two other biological preparations. Isolated frog hearts showed enhanced calcium ion efflux at SARs of 0.00015 and 0.0003 W/kg when exposed to 240 MHz, amplitude modulated at 16 Hz (Schwartz et al., 1990). Human neuroblastoma cells exposed in culture to amplitude modulated 147 and 915 MHz at SARs of 0.005 and 0.05 W/kg displayed maximal calcium ion efflux at modulation frequencies around 16 and 60 Hz (Dutta et al., 1984, 1989). The latter experiment was conducted under natural, cell-culture growth conditions and suggests that anoxia is not an absolute requirement for sensitivity of nervous system derived cells to RF fields modulated at ELF frequencies.

Overall, the exposure-induced release of calcium ions from tissues should be viewed as contributing to the characterization of exposure conditions required to elicit a response, and, thus, to the development of an underlying mechanism of action. The efflux assay system may ultimately be useful in defining the various aspects of the physical and biological exposure conditions that sensitize and affect membrane responses to electromagnetic field exposure. It should be emphasized that insufficient information is available to define the weak field interactions. Furthermore, the reported effects cannot be characterized as a potential adverse effect on health, since little or no confirmed information has been gathered that suggests this effect occurs in animals or humans.

6.5 Indirect interactions

Electromagnetic fields, at frequencies below about 100 MHz, interact with biological bodies through electrical charges induced on ungrounded or poorly grounded metallic objects, such as cars, trucks, cranes, wires, and fences.

Two types of interaction may occur:

(*a*) a spark discharge before a person touches the object;

(*b*) the passage of current to ground through a person coming into contact with such objects; the magnitude of these currents depends on the total charge on the object. This charge, in turn, depends on the frequency and electric field strength, the object geometry and capacitance, and the person's impedance to ground.

Above a certain threshold, the current to ground is perceived by the person as a tingling or prickling sensation in the finger or hand touching the charged object, for frequencies below about 100 kHz, and as heat at higher frequencies. A severe shock can be experienced at levels much higher than this threshold. The threshold currents depend on frequency, surface of contact area, and the individual. The thresholds for effects (perception, shock, etc.) are generally higher for men than for women and children, though there are also individual differences.

All effects due to induced charges on objects are defined below in order of increasing severity:

Perception - The person is just able to detect the stimulus. There is a difference in the current perception threshold for touch and grip contact.

Annoyance - The person would consider the sensation to be a mild irritant, if it were to occur repeatedly.

Startle - If a person receives one exposure, it is sufficient to motivate the person to avoid situations that would lead to a similar experience.

The remaining reactions apply only to contact of alternating currents at frequencies below 100 kHz.

Let-go - A person cannot let go of a gripped conductor as long as the stimulus persists, because of uncontrollable muscle contraction. If a person is exposed to prolonged currents, somewhat above the let-go level, through the chest, breathing becomes difficult and, eventually, the person may become exhausted and die.

Respiratory tetanus - A person is unable to breathe as long as the stimulus is applied, owing to the contraction of the muscle responsible for breathing.

Fibrillation - Uncoordinated asynchronous heart contractions produce no blood pumping action.

Threshold currents for their occurrence are given in Table 7. Fig. 14 and 15 show threshold currents for perception and let-go, for different percentages of the population at lower frequencies. Thresholds for perception and pain (well below the let-go) were evaluated for nearly 200 men and 200 women and also estimated for 10-year-old children (Chatterjee et al., 1986). The thresholds are lower for finger contact than for grasping contact. Fig. 16 and 17 show perception and pain for finger contact (Chatterjee et al., 1986). The stimuli in both cases are tingling/pricking at frequencies below about 100 kHz and heat/warmth at higher frequencies.

Currents flowing from an object to ground through a person who touches the object can be reduced if shoes are worn (Chatterjee et al., 1986). Electric charge induced on various objects and, therefore, contact currents for people, can be calculated for a known electric field strength. Results of such calculations are shown in Fig. 18 and 19 for finger contact for males, females, and children, respectively.

RF burns can occur when current enters through a small cross-section of the body, such as a finger, when the finger contacts an electrically charged object. Another interaction that may occur at lower frequencies is a transient discharge, which occurs between a person and a charged object either by direct contact or through an air gap (Tenforde & Kaune, 1987).

Table 7. Threshold currents (mA) for various effects at frequencies ranging from 50 Hz to 3 MHz (experimental data for 50% of men, women, and children)

Effect	Subject	Threshold current (mA) at various frequencies								
		50/60 Hz	300 Hz	1000 Hz	10 kHz	30 kHz	100 kHz	300 kHz	1 MHz	3 MHz
Touch perception (finger contact)	men	0.36	(0.47)	(0.79)	4	15	40	40	40	40
	women	0.24	(0.31)	(0.53)	3.2	12	35	35	35	35
	children	*0.18*	*0.24*	*0.40*	2.5	8	25	25	25	25
Grip perception	men	1.1	1.3	2.2	15	50	300	300	300	300
	women	0.7	*0.9*	*1.5*	10	35	200	200	200	200
	children	*0.55*	*0.65*	*1.1*	9	30	150	150	150	150
Shock, not painful (grasping contact)	men	1.8	(2.3)	(3.2)	17(10)	(25)	(25)			
	women	1.2	*1.5*	*2.1*	11	*16.7*	*16.7*			
	children	*0.9*	*1.1*	*1.6*	*8.5*	*12.5*	*12.5*			
Pain (finger contact)	men	(1.8)	(2.4)	(3.3)	10	30	55	50	50	50
	women	*1.2*	*1.6*	*2.2*	6.5	23	47	45	40	40
	children	*0.9*	*1.2*	*1.6*	6	18	33	30	28	28
Shock, painful; muscle control (let-go threshold for 0.5% of population)	men	9	(11.7)	(16.2)	55	(126)	(126)			
	women	6	*7.8*	*10.8*	37	*84*	*84*			
	children	4.5	*5.9*	*8.1*	27	*63*	*63*			

Table 7 (*continued*)

Effect	Subject	Threshold current (mA) at various frequencies								
		50/60 Hz	300 Hz	1000 Hz	10 kHz	30 kHz	100 kHz	300 kHz	1 MHz	3 MHz
Burn (finger contact)	men								200	200
Painful shock, let-go threshold	men	16	18	24	75(88)	(224)	(224)			
	women	10.5	*12*	*16*	*50*	*150*	*150*			
	children	*8*	*9*	*12*	*37*	*112*	*112*			
Severe shock, breathing difficulty	men	23	(30)	(41)	94(126)	(320)	(320)			
	women	15	*20*	27	63	*214*	*214*			
	children	*12*	*15*	*20.5*	*47*	*160*	*160*			

[a] From Dalziel 1954a,b; Deno, 1974; Guy & Chou, 1982; Guy, 1985; Chatterjee et al., 1986). Data in brackets were calculated by using the frequency factors for perception thresholds and for pain and let-go thresholds, given in IEC Publication 479. Data in italics were calculated by assuming thresholds for women two-thirds of that of men and thresholds for children one-half of that for men (IEEE, 1978; Guy, 1985).

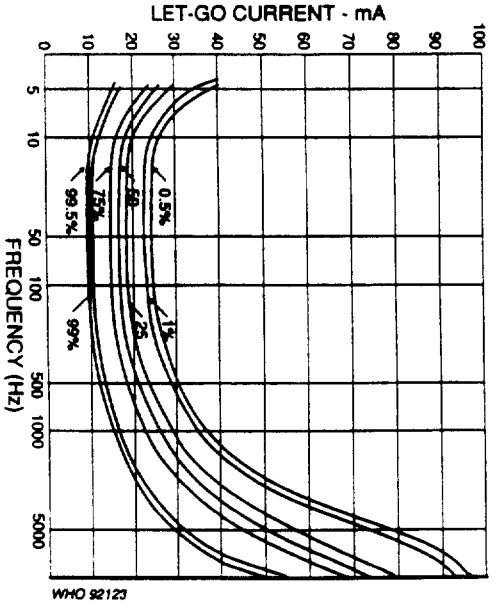

Fig. 15. Let go currents for different percentages of the population. From: EPRI (1979).

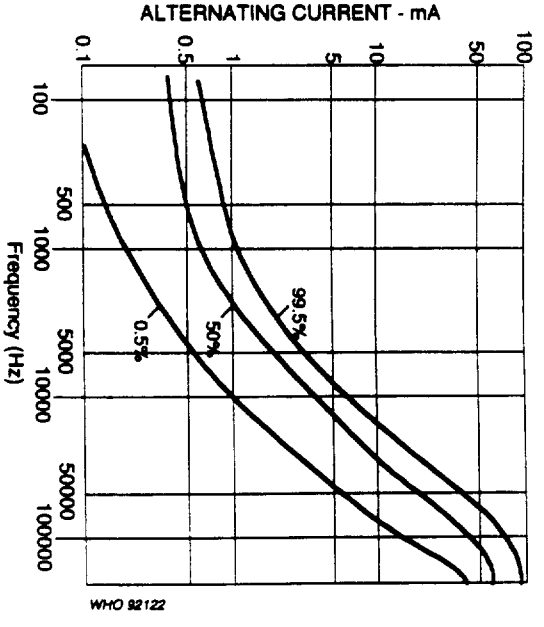

Fig. 14. Threshold currents for perception by various percentages of the population. From: EPRI (1979).

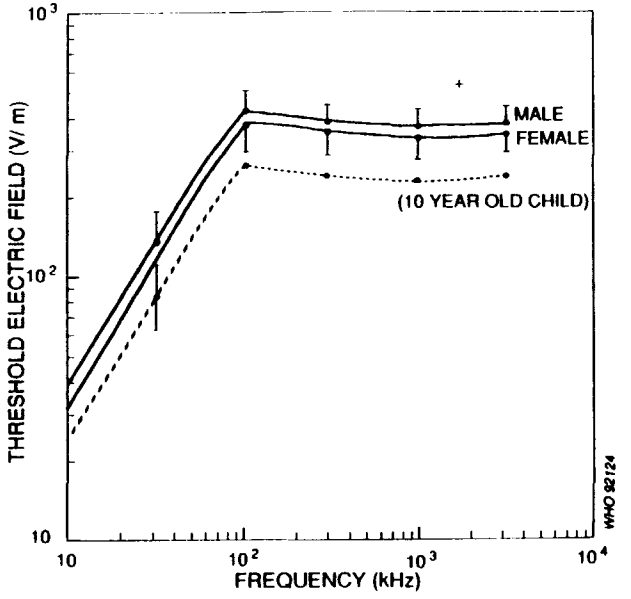

Fig. 16. Average threshold current for perception, finger contact, for adult males, females, and 10-year-old children (estimated). From: Chatterjee et al. (1986).

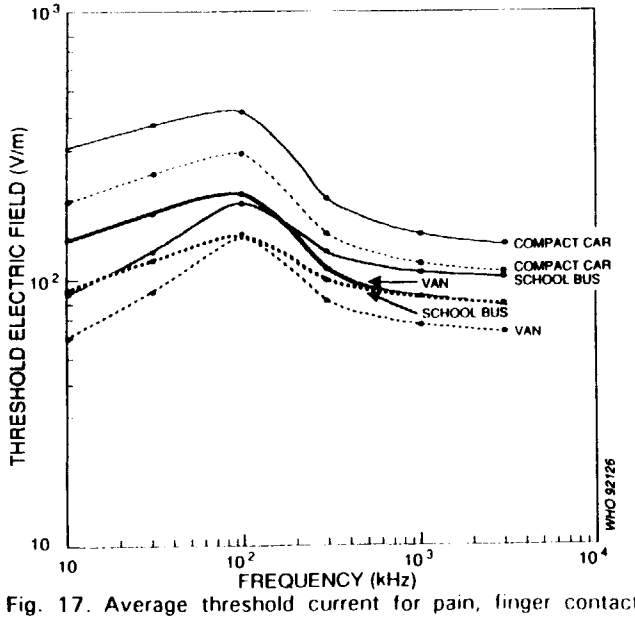

Fig. 17. Average threshold current for pain, finger contact. From: Chatterjee et al. (1986).

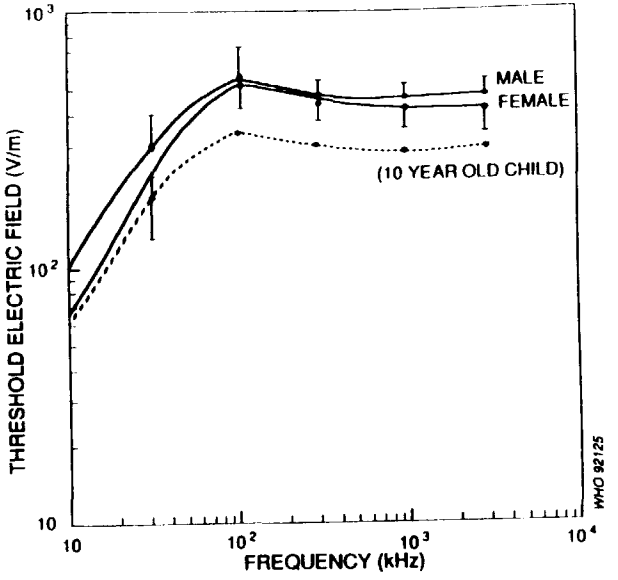

Fig. 18. Average threshold electric field for perception for grounded adult males (solid lines) and 10-year-old children (dashed line) in finger contact with various vehicles. From: Chatterjee et al. (1986).

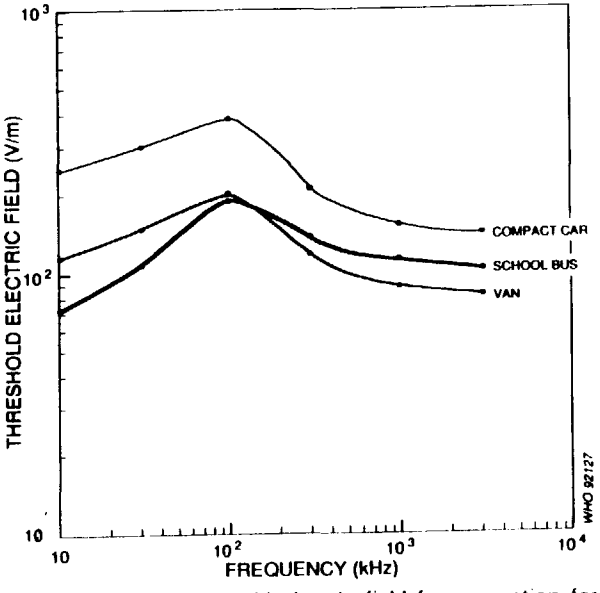

Fig. 19. Average threshold electric field for perception for grounded females in finger contact with various vehicles. From: Chatterjee et al. (1986).

7. CELLULAR AND ANIMAL STUDIES

7.1 Introduction

Numerous reviews and monographs dealing with the biological effects of electromagnetic fields have been published including: WHO (1981); Grandolfo et al. (1983); USEPA (1984); Akoev (1986); NCRP (1986); Polk & Postow (1988); Francescretti et al. (1989); WHO (1989); Adey (1989, 1990); Saunders et al. (1991). The purpose of this section is to provide an overview of the biological effects that are relevant to considerations of the health and safety of exposed people.

The available scientific data are unevenly distributed within the very broad range of frequencies that this publication covers. Considerable numbers of *in vitro* and experimental animal studies have been performed in the mega- and gigahertz range. Relatively few scientific reports of effects in the kilohertz range can be found and data are particularly sparse for the range between 300 Hz and about 10 kHz.

7.2 Macromolecules and cell systems

Studies of isolated (*in vitro*) components of a biological system offer possible insights into the mechanisms of RF action. *In vitro* systems are simple, allowing biological variables to be controlled and subtle effects to be identified without being masked by the homeostatic responses of the whole organism.

In addition, the precise control of the temperature of *in vitro* preparations during exposure should make it possible for thermal and athermal interactions to be clearly distinguished, though thermal gradients cannot be entirely eliminated from such systems. Effects to be tested *in vivo* (whole animal) can be identified from these studies.

From their review of RF effects on macromolecular and cellular systems, NCRP (1986) concluded that RF fields, at least continuous waves at frequencies above 5 MHz, have little, if any, effect on biopolymers, cell organelles, and microorganisms, other than effects associated with elevated temperatures. Likewise, they concluded that the effects of RF fields on the genetic material of cells have not been

convincingly demonstrated, unless related to elevations of temperature.

More recently, Cleary (1989) noted that there was strong evidence from a number of *in vitro* experiments for the involvement of non-thermal RF interactions, as well as heating. He concluded that effects that may be attributed to RF-specific interactions include altered potassium and sodium ion transport across red blood cell membranes, changes in membrane calcium ion fluxes, decreased non-cAMP-dependent protein kinase activity, inhibition of T-lymphocyte cytotoxicity, biphasic effects on lymphocyte proliferation, changes in brain cell energy metabolism, altered firing rates and resting potentials of neurons, and effects on cell transformation rate. Many of these responses are discussed below.

7.2.1 Effects on cell membranes

The cell membrane has been suggested as a likely site for the interaction of RF fields (Adey, 1981; Cleary, 1987). Several studies (summarized in Table 8) have focused on effects on membrane permeability and integrity.

Baranski et al (1971) reported increased cation permeability and decreased osmotic resistance in rabbit erythrocytes exposed to 3 GHz for up to 3 h at power densities as low as 10 W/m^2; higher power densities produced effects of greater magnitude. Using thermal controls heated in a waterbath to the same temperature as exposed cells, Hamrick & Zinkl (1975) were unable to replicate these effects. Liu et al. (1979) attributed observed increases in cation permeability of erythrocytes to heating.

More recently however, it has been reported in several studies that exposure to RF fields caused specific increases in the cation permeability of the cell membrane. The results of these studies have been consistent with a sensitivity of the cell membrane at particular temperature-dependent energetic states; in some studies, effects have been reported only at apparent membrane phase transition temperatures (between 8 °C and 36 °C). Membranes loaded with cholesterol to eliminate the phase transition were unaffected by microwaves (Liburdy & Vanek, 1987). RF-induced changes in the activity of the membrane-bound enzyme Na/K ATPase have been suggested as a possible mechanism (Allis & Sinha-Robinson, 1987),

but similar permeability changes have been reported in membranes with no associated protein (Liburdy & Magin, 1985).

Table 8. Membrane studies (*in vitro*)

Exposure condition	Effect	Reference
3 GHz (CW) at 10-100 W/m^2, for up to 3 h	Increased K^+ efflux and decreased osmotic resistance in rabbit erythrocytes compared with room temperature controls (increased effect at higher power densities)	Baranski et al. (1974)
2.45 or 3 GHz (CW) at 40-750 W/m^2 (3-57 W/kg), for up to 3 h	No effects on K^+ efflux or osmotic resistance in rabbit erythrocytes compared with thermal controls	Hamrick & Zinkl (1975)
2.45, 3 and 3.95 GHz (CW) at up to 200 W/kg (26 - 44 °C)	Increased K^+ ion and haemoglobin release and osmotic lysis by rabbit, canine, and human erythrocytes; similar effects with conventional heating	Liu et al. (1979)
2.45 GHz, at up to 390 W/kg, for 1 h	Increased passive efflux of Na^{22} and Rb^{86} from rabbit erythrocytes compared with thermal controls, only at the transition temperatures for efflux (8-13 °C, 22.5 °C and 36 °C)	Olcerst et al. (1980)
8.42 GHz, CW or pulse modulated, for 2 h, at up to 90 W/kg (23-28 °C)	Increased K^+ efflux from rabbit erythrocytes relative to thermal controls at around 24 °C	Cleary et al. (1982)
2.45 GHz (CW) at 2-3 W/kg for up to 2 h (7-35 °C)	Increased Na^+ efflux from human erythrocytes compared with thermal controls at 22-25 °C	Fisher et al. (1982)

Table 8 (*continued*)

Exposure condition	Effect	Reference
2.45 GHz (CW) at 60 W/kg, for 30 min (15-24 °C)	Increased passive Na^+ transport and protein shedding from rabbit erythrocytes compared with thermal controls, only at membrane phase transition temperatures of 17.7-19.5 °C	Liburdy & Penn (1984)
2.45 GHz (CW) up to 100 W/kg, for up to 60 min (13-43 °C)	Increased Na^+ permeability of rabbit erythrocytes compared with thermal controls, only at 17.7-19.5 °C; response abolished in cholesterol-loaded membranes with no apparent phase transition	Liburdy & Vanek (1987)
1.0 GHz (CW) at up to 15 W/kg, for up to 5 h (15-40 °C)	No effect on membrane fluidity of human erythrocytes, as measured by lateral diffusion of lipophilic dye	Allis & Sinha (1981)
2.45 GHz (CW) 6 W/kg, for 20 min (23-27 °C)	Inhibition of Na/K ATPase activity in human erythrocyte ghosts, only at 25 °C	Allis & Sinha-Robinson (1987)

7.2.2 *Effects on haematopoietic tissue*

A summary of *in vitro* studies conducted to determine haematopoietic and immunological end points is shown in Table 9. In general, these studies show that RF exposure, under temperature-controlled conditions, at SARs up to 28 W/kg have no effects on cell survival or mitogen-stimulated lymphoblastoid transformations.

In some studies, effects are reported at levels too low to involve significant heating, or at certain RF modulation frequencies. In one unreplicated study, depressed phagocytosis was reported in RF-exposed mouse macrophages. A slight rise in temperature in the

culture medium would have tended to increase activity. T-lymphocyte cytotoxicity was depressed during low-level exposure to 450 MHz RF modulated at frequencies of 16 and 60 Hz, but not at other frequencies. In other studies, a lack of effects of sinusoidal or pulse-modulated RF fields on B-lymphocyte capping in mouse spleen cells, viability, and DNA synthesis in human mononuclear lymphocytes has been reported.

Table 9. Haematopoietic and immunological studies (*in vitro*)

Exposure conditions	Effect on exposed group	Reference
Colony-forming ability		
2.45 GHz (CW) up to 2 kW/kg, for 15 min	Dose-related, reduced colony-forming ability of mouse bone marrow cells - temperature kept constant; direct effect of RF on haematopoietic precursor	Lin et al. (1979)
2.45 GHz (CW), 2.4 kW/m^2, for 5 min; rise in temperature of mouse bone marrow suspension was from 20 to 45 °C	cells; spleen colonies in radiation-depleted recipients rose when temperature rose to between 33 and 40 °C, but fell above 41 °C	Rotkovska et al. (1987)
Mitogen responses		
2.45 GHz (CW), 19 W/kg, for 1-4 h, temperature controlled at 37 °C	No changes in cell viability or blastogenic responses of mouse spleen lymphocytes to several mitogens	Smialowicz (1976)
2.45 GHz (CW), up to 28 W/kg for up to 44 h, constant temperature of 37 °C	No effects on spontaneous or mitogen-stimulated transformation of rat lymphocytes	Hamrick & Fox (1977)
2.45 GHz (CW) up to 4 W/kg, temperature rise of 0.9 °C	No effects on human leukocytes viability or on unstimulated or mitogen-stimulated lymphoblastoid transformation	Roberts et al. (1983)

Table 9 (*continued*)

Exposure conditions	Effect on exposed group	Reference
Modulated RF		
450 MHz, 15 W/m^2, sinusoidal-modulated at 3, 16, 40, 60, 80, 100 Hz	Suppression of mouse T-lymphocyte cytotoxicity, peak at 60 Hz (20%)	Lyle et al. (1983)
147 MHz, pulse-modulated at 9, 16, 60 Hz, 1.1-480 W/m^2	No change in mouse spleen B-lymphocyte capping as temperature maintained constant	Sultan et al. (1983b)
2.45 GHz, pulse-modulated at 16 or 60 Hz, up to 4 W/kg	No effects on human lymphocyte viability, unstimulated or mitogen-stimulated DNA synthesis, or total protein synthesis	Roberts et al. (1984)
Pulsed 9 GHz (1000 pps) 200 W/m^2 amplitude-modulated at 16 MHz (100% mod.) and 16 Hz (5% mod.) plus 0.8 Hz magnetic field 60 mT, 12 h per day, for 5days	Decrease in no. of plaque-forming cells and cytotoxicity of NK cells in mice	Bottreau et al. (1987)
Other		
2.45 GHz (CW), 500 W/m^2, for 30 min, temperature rise of 2.5 °C but below optimum temperature for phagocytic activity	Depression of phagocytosis in peritoneal mouse macrophages	Meyers & Habershaw (1973)
2.45 GHz (CW), for 30 min, up to 1 kW/m^2 (SAR up to 45 W/kg)	Ability of normal mouse B-lymphocytes to form a "cap" on the plasma membrane of antigen-antibody complex reduces with increasing temperature; if temperature kept constant, no difference between exposed and control cells	Sultan et al. (1983a)

7.2.3 Isolated cerebral tissue, peripheral nerve tissue, and heart preparations

Studies carried out on calcium ion exchange in chick cerebral tissue preparations and other tissues exposed to RF fields, amplitude modulated at ELF frequencies, are described in section 6 on interaction mechanisms.

Table 10. Peripheral nervous tissue studies

Exposure conditions	Effect on exposed group	Reference
2.45 GHz (CW or pulsed), 1 kW/kg, for several minutes, temperature controlled	No effect on compound action potential in functioning isolated frog and cat nerves or peripheral autonomic ganglia of rabbits	Chou & Guy (1973); Courtney et al. (1975)
1.5 or 2.45 GHz (CW), few minutes above threshold of approx. 5 W/kg	Reversible changes in firing pattern of pacemaker neurons of *Aplysia*	Wachtel et al. (1975)
2.45 GHz (CW or pulsed), temperature controlled above a threshold of 5-10 W/kg, for 30 min	Prolongation of refractory period of isolated frog sciatic nerves	McRee & Wachtel (1980, 1982)

Studies conducted on peripheral nerve tissue are summarized in Table 10. Most effects of RF exposure on the properties of isolated nerve preparations can be ascribed to heating. For example, the changes seen in the firing pattern of pacemaker neurons in Aplysia, exposed at 5 W/kg or above (Wachtel et al., 1975), were considered to be consistent with heating (Seamen, 1977). However, in two studies, changes were reported in the properties of frog nerves exposed above 5-10 W/kg, under constant temperature conditions. These changes were not induced by exposure to infrared radiation, suggesting an athermal response. The authors noted, however, that, even under temperature-controlled conditions, thermal gradients were difficult to eliminate.

Several studies (reviewed by Liddle & Blackman (1984) and NCRP (1986) have been performed on isolated heart preparations. Decreases in heart rate (bradycardia) have been reported in isolated turtle, frog, and rat heart preparations exposed to RF at intensities as low as 15 W/m^2 (NCRP, 1986). However, Clapman & Cain (1975) indicated that at least some of the effects observed with these preparations may have been caused by currents induced in electrodes in contact with the myocardia. Some support for this comes from the work of Yee et al. (1984), though a later study (Yee et al., 1988) also implicated the low temperatures and oxygen levels used in these experiments.

7.2.4 Mutagenic effects

Numerous tests have been carried out to examine the potential mutagenic action of RF field exposure. In general, no changes in mutation rate have been observed, except in cases where substantial temperature increases may also have occurred (USEPA, 1984; NCRP 1986).

Studies of the chromosomal effects resulting from RF exposure of somatic cells are summarized in Table 11. Most well-conducted studies report a lack of effect on chromosome aberration frequencies or sister chromatid exchange rates, even when RF exposure produces mild hyperthermic conditions. Increased aberration frequencies were reported in one isolated, long-term study of rat kangaroo cells exposed for 50 passages (over 320 days) to 2.45 GHz at 15 W/kg. However, these results may have been confounded by temperature and senescence (aging) in the cell populations.

Table 11. Mutagenic effects in somatic cells

Exposure conditions	Effect on exposed group	Reference
20 kHz sawtooth magnetic field, 16 μT pk-pk, for 72 h	Non-significant ($P=0.06$) increase in chromosome aberration frequency in human amniotic cells, DNA synthesis reduced	Nordessen et al. (1989)
2.45 GHz (CW), up to 200 W/kg, for 20 min temperature rose from 4 °C or 23 °C to 36 °C during exposure, second experiment temperature rose from 37 °C to 40 °C.	Human blood lymphocytes showed no increase in unstable chromosome or sister chromatid exchanges	Lloyd et al. (1984, 1986)
2.45 GHz (CW) 15 W/kg, for up to 320 days (50 passages)	Increased chromosome aberrations and polyploidy and decreased growth rate in rat kangaroo RH5 and RH16 cells	Yee (1982)

7.2.5 Cancer-related studies

Experiments on cell systems exposed to RF that have end points related to cancer are shown in Table 12. Cellular transformation studies are important assays of potential carcinogenicity, in which the potential is examined of a suspect carcinogen to abolish contact inhibition, an important regulator of cell division. They are, however, very susceptible to factors such as variation in growth media. Balcer-Kubiczek & Harrison (1985, 1989) reported enhanced transformation rates in mouse fibroblasts after RF exposure for 24 h at 4.4 W/kg (alone or combined with X-radiation), followed by treatment with the chemical promotor TPA. These experiments are not conclusive; there were inconsistencies between the studies in plating efficiency and in the response to RF combined with X-radiation. The authors also noted that the transformation rates were susceptible to temperature changes. However, these studies are important and should be replicated.

Protein kinases and ornithine decarboxylase are enzymes important in normal and neoplastic cell growth and division. Byus et al. (1984) reported an effect of exposure to amplitude-modulated RF on cAMP-independent kinase, but no effect on cAMP-dependent

Table 12. Cancer-related studies (*in vitro*)

Exposure conditions	Effect on exposed group	Reference
2.45 GHz (CW), 4.4 W/kg for 24 h, temperature constant at 37 °C	RF reduced plating efficiency of mouse embryo fibroblasts to half, but no effect on transformation rate was induced by treatment with benzopyrene or X-rays alone. Exposure of cells to RF and X-rays, then tumour promotor (phorbal ester TPA), caused a several-fold increase in transformation frequency compared with cells exposed to X-rays and treated with TPA	Balcer-Kubiczek & Harrison (1985)
2.45 GHz (CW), 4.4 W/kg for 24 h, temperature constant at 37 °C	Increased mouse embryo fibroblast transformation rate per surviving cell, in cells exposed to RF with, or without X-rays, and then treated with TPA. In contrast to 1985 study, no effect on cell plating efficiency or difference in transformation response to combined X-ray, RF and TPA compared with X-ray & TPA alone	Balcer-Kubiczek & Harrison (1989)
450 MHz, pulse-modulated at 3-100 Hz, 10 W/m^2, for up to 60 min	No effect on human lymphocyte cAMP-dependent protein kinase activity. cAMP-independent kinase activity fell to less than 50% of control levels after 15-30 min exposure, then returned to control levels at 45-60 min. Reduced enzyme activity occurred at 16, 40, 60 Hz modulation, not at 3, 6, 80 or 100 Hz, or unmodulated carrier	Byus et al. (1984)
450 MHz amplitude-modulated, 10 W/m^2, for 1 h	Increased ornithine decarboxylase (ODC) at 10, 16, 20 Hz modulation by Reuber H35 hepatoma cells, CHO cells, and human melanoma cells; RF (modulated at 16 Hz) exposure of CHO and hepatoma cells potentiated a TPA induced increase in ODC, but not in DNA synthesis in TPA-treated cells	Byus et al. (1988)

kinase, normally implicated in cellular responses leading to proliferation. Amplitude-modulated RF exposure was also found to enhance ornithine decarboxylase activity in several different cell lines (Byus et al., 1988), though only by a small amount compared with chemical promotors. No effect was seen on DNA synthesis (assayed 14 h after exposure), which is a subsequent step in the promotional sequence. It is not possible to draw any conclusions with respect to cancer from these studies.

7.2.6 *Summary and conclusions:* in vitro *studies*

The results of *in vitro* studies, conducted so far, suggest that the cell membrane is a site of interaction of RF fields and that alterations in membrane permeability can result, as well as changes in membrane cation fluxes, changes in the activity of certain enzymes, and suppression of some immune responses. RF fields are not mutagenic; an effect on cellular proliferation, particularly in relation to tumour promotion, by interactions other than tisue heating, has not been established. Evidence is presented that some effects may result from athermal interactions, particularly in response to amplitude-modulated fields. However, in many other cases, there is great difficulty in eliminating thermal gradients within exposure samples exposed at high levels.

7.3 Animal studies

While *in vitro* studies are important in determining the mechanisms of interaction and identifying appropriate biological end-points and exposure conditions to be tested in whole animals, they cannot serve as a basis for health risk assessment in humans. Whole animal studies are necessary in order to evaluate the integrated response of various systems of the body that serve to maintain homeostasis, the condition necessary for the proper functioning of the body. Three bodily systems can be identified as of particular importance in this respect: the nervous, endocrine, and immune systems. The coordinated interdependent interaction of these systems in response to chemical and physical stimuli provides a great capacity for adaptation and compensation in response to changes in environmental or internal bodily conditions.

Local hyperthermia, caused by exposure to strong RF fields, and damage to morphological structures of the above systems, can lead,

in turn, to physiological deregulation. Exposure to weaker RF fields with minimal thermal loading can result in adaptive and compensatory shifts of these homeostatic mechanisms.

Another important end-point in the consideration of human health and safety concerns the possible effects on reproduction, and on pre- and post-natal development. In this context, the induction of mutagenic changes in germ cells by RF exposure might result in hereditary effects in offspring. In somatic cells, such changes could be associated with the induction of cancers.

The effects of exposure to RF fields on these various biological end-points is described in the following sections. It is important to note that, as far as thermal responses are concerned, experimental interpretation can be confounded by differences in ambient temperature, relative humidity, and air flow. In addition, the thermal load induced by a given SAR is different in different animals, generally increasing with body weight in small animal species. These two points have been evaluated by Gordon et al. (1986) and Gordon (1987), who argue for a conservative extrapolation of thermal effects from laboratory animals to humans.

7.3.1 *Nervous system*

Studies of the effects of RF exposure on the nervous system are shown in Table 13. Results of early studies suggested that the blood-brain barrier (which regulates cerebro-spinal fluid composition) was possibly susceptible to RF field exposure. For example, Frey et al. (1975) reported the penetration of the blood-brain barrier of anaesthetised rats by fluorescein after low-level, pulsed or CW exposure. Oscar & Hawkins (1977) reported increased permeability to radiolabelled saccharides after exposure of anaesthetized rats to low-level RF. However, later work (reviewed by Blackwell & Saunders, 1986; NCRP 1986) indicated that these responses may have been confounded by various factors, including alteration in cerebral blood flow, the effect of the anaesthetic, and changes in renal clearance.

The uptake of horseradish peroxidase by brain tissue is less susceptible to these factors. Increased uptake reported in conscious Chinese hamsters after exposure at 2 W/kg (Albert, 1977); decreased uptake has been reported at higher SARs (Williams et al., 1984b,d).

Table 13. Nervous system effects

Exposure conditions	Effect on exposed group	Reference
450 MHz (amp. mod. 16 Hz), for 60 min, to 30 W/m^2 (33 V/m, SAR: 0.29 W/kg)	Altered exchange rate of Ca^{++} during and after exposure of cat cortex	Adey et al. (1982)
2.06 GHz (CW or pulsed 18, 6, 32 Hz), 5-100 W/m^2 (SAR 0.12-2.4 W/kg)	No change in Ca^{++} mobility in rat cerebral tissue	Merritt et al. (1982)
2.45 GHz pulsed (2 μs pulses at 500 Hz) or CW for 45 min (SAR 0.6 W/kg)	Decreased choline uptake in the rat brain tissue; effect depended on exposure parameters	Lai et al. (1988)
2.45 GHz (pulsed - 2 μs pulses at 500 Hz) for 45 min. (SAR 0.3-1.2 W/kg)	Decreased choline uptake in the rat brain tissue at 0.45 W/kg and above	Lai et al. (1989)
915 MHz (CW), 10-400 W/m^2, for 15 min exposure of head (SAR threshold 2.5-5 W/kg)	Decreased latency of late components only evoked potentials in thalamus of cats	Johnson & Guy (1972)
147 MHz (amplitude-modulated 1-25 Hz) 10 W/m^2 (approx SAR 0.015 W/kg)	Altered EEG responses in cats exposed to field modulated at EEG frequencies	Bawin et al. (1973, 1974)
2.95 GHz, single or repeated exposure up to 50 W/m^2 (SAR 1 W/kg) 2 h/day for 3-4 months	EEG of rabbits unaffected by acute exposure; desynchronization of EEG from long-term exposure; pulsed (1 μs pulses at 1200 Hz) more effective for changes than CW	Baranski & Edelwejn (1975)
3 GHz (1 μs pulses at 500-699 Hz) 50 W/m^2 (SAR 1 W/kg) in rats, for 10 days	Transient enhancement of EEG at frequency of pulse repetition rate, persisted after exposure ceased	Servantie & Etienne (1975)
1-10 MHz (amplitude-modulated 14-16 Hz) E field 500 V/m, 2 h/day, for 6 weeks	Sustained changes in EEG after 2-3 weeks of exposure of rabbits	Takashima et al. (1979)
1-30 MHz (amplitude-modulated 60 Hz) single exposure, for 3 h	No effect	
500 MHz - 3GHz 25-50 W/m^2, for 15 days, at 0.5-1 W/kg	No effects on EEG in rats and monkeys	Klein et al. (1985)

Table 13 (*continued*)

Exposure conditions	Effect on exposed group	Reference
4 GHz, CW or amplitude-modulated at 16 Hz (70% mod.), for 30 min (SAR in cortex 8.4, 16.8, or 42 W/kg)	Slight changes in EEG pattern, particularly at 16.8 W/kg amplitude-modulated RF and 42W/Kg CW	Mangel et al. (1990)

More recently, changes in blood-brain barrier permeability have been reported after exposure to MRI field conditions; however, the evidence for an effect is contradictory, at present (Prato et al., 1990; Ross et al., 1990).

Pulsed RF fields appear to have various effects on the nervous system. Exposure to very high peak power pulses is reported to suppress startle reflex and evoke body movements in conscious mice (Wachtel et al., 1988; 1989). For evoked body movement, each pulse (10 μs in duration) produced a mid-brain specific absorption of around 200 J/kg, corresponding to an SAR of 20 MW/kg and was estimated to lead to a rise in mid-brain temperature of 0.05 °C. Pulsed fields were only about twice as effective as CW suggesting that the effect is unlikely to be due to thermoelastic mechanisms.

Pulsed RF exposure of rats for 45 min at SARs as low as 0.45 W/kg has been shown to affect the sodium-dependent, high affinity choline uptake (an indicator of cholinergic activity) in different parts of the brain (Lai et al., 1989). In a previous study, Lai et al. (1988) found that the effect varied with different exposure parameters. Further work (Lai et al., 1990) revealed that the concentration of benzodiazepine receptor (involved in anxiety and stress responses) in the brain of rats exposed for 45 min to pulsed 2.45 GHz or whole body SARs of 0.6 W/kg was increased in some parts of the brain, immediately after exposure. However, the effect diminished with repeated exposure over a 10-day period. The authors suggested that the data support the hypothesis that low-level RF exposure is a mild nonspecific stressor. There are a number of responses (heat, noise) that can be regarded as nonspecific stressors. This set of studies needs further elaboration to identify the extent and mechanisms of the stress involved, before its implication for health risk can be assessed. High levels of RF, sufficient to raise spinal or

thalamic temperatures by several degrees Celsius, decreased the latency of late components of thalamic evoked potentials.

Exposure to low levels of amplitude-modulated RF has been reported to alter brain activity (measured using electro-encephalography) and to affect calcium ion mobility in the cortex. Exposure to 147 MHz fields, amplitude-modulated between 1 and 25 Hz, has been reported to affect the ability of cats to produce selected EEG rhythms. Changes have also been reported in the EEG frequency spectrum in rabbits exposed to long-term 1-10 MHz, amplitude-modulated at 14-16 Hz.

Small changes in EEG patterns, particularly earlier studies on desynchronisation, were reported in rats and rabbits, after exposure to an SAR at around 1 W/kg (Baranski & Edelwejn, 1975; Servantie & Etienne, 1975). However, later studies reported a lack of effect.

The exposure of cats at about 0.3 W/kg to 450 MHz, amplitude-modulated at 16 Hz, has been reported to alter calcium ion mobility in the cortex (measured as the efflux of labelled calcium ions from the cortex surface) (Adey et al., 1982). In contrast, exposure at between 0.12 and 2.4 W/kg to 2.06 GHz, pulse-modulated at 8, 16, or 32 Hz, was reported to have no effect on calcium ion exchange in the rat cortex (Merritt et al., 1982).

Exposure to RF has been shown by several authors to influence the effects of various neuroactive drugs (see Table 14). Acute and long-term exposure have been reported to potentiate the effects of stimulant and convulsant compounds (Baranski & Edelwejn, 1974; Servantie et al., 1974). Thermally significant exposures have been reported to decrease the period of barbituate-induced anaesthesia in mice and rabbits; Blackwell (1980) suggested thermally enhanced redistribution from brain tissue as a probable mechanism.

7.3.2 Ocular effects

The lens of the eye is potentially sensitive to RF exposure, because it lacks a blood supply and so has a reduced ability to dissipate heat compared withto other tissues. In addition, the fibres that make up the bulk of the lens have only a limited capacity for repair and tend to accumulate the effects of minor insults.

Table 14. Nervous system effects with drugs

Exposure conditions	Effect on exposed group	Reference
1.7 or 2.45 GHz (CW) up to 500 W/m^2 (up to 10 W/kg)	Rabbits injected with sodium pentobarbital and exposed to RF showed reduced sleeping times; correlated with increased rectal temperature	Cleary & Wangemann (1976)
2.45 GHz (CW), 250 W/m^2 and above (SARs >17 W/kg) (rectal temperature rise 3 °C)	SAR dependent reduction in hexobarbital-induced sleeping time in mice during RF exposure	Blackwell (1980)
3 GHz (CW) 70 W/m^2 (1.2 W/kg) for 3 h/day, for 200 h exposure	Variable effect on chlorpromazine and pentylen-etetrazol changes in EEG activity in rabbits	Baranski & Edelwejn (1974)
3 GHz (pulsed 1 μs at 525 Hz), for unspecified duration, each day for 8-35 days, at 5 W/kg	Variable latency of response to pentylenetetrazol induction of convulsion activity	Servantie et al. (1974)
9.3 GHz (CW), 7-28 W/m^2 0.6 W/kg, for 5 min	No differences in EEG from normal sodium pentobarbital anaesthetic action	Goldstein & Sisko (1974)

Most experimental work on the RF induction of cataracts (see Tables 15 and 16) has been carried out using near-field exposures at 2.45 GHz, to selectively irradiate the eye or the side of the head, in order to avoid whole-body thermal stress. The intense exposures used in these studies have often led to other effects, such as lacrimation and oedema of surrounding tissue.

Exposure has usually been well above perception threshold and the animals have usually been anaesthetised. In most studies, the rabbit has been used as the experimental animal model, because the dimensions of its eye approach those of the human eye.

Different conditions of exposure can affect the type of opacity formed or be ineffective in inducing any permanent change. The efficacy with which the applied RF field can induce cataracts depends on the depth of penetration and hence the frequency. Below 1.5 GHz, the dimensions of the orbit-eye combination are too small to result in local field concentration. Above about 10 GHz,

Table 15. Ocular effects from acute exposure

Exposure conditions	Effect on exposed group	Reference
Rabbits		
2.45 GHz (CW); 4.2 kW/m^2, for 5 min, or 1.5 kW/m^2, for 60 min	Posterior cortical opacities within a week; first visible changes (milky bands) 1-2 days after exposure	Carpenter & VanUmmerson (1968)
2.45 GHz (CW); up to 2.5 kW/m^2 repetitive exposure	Ultrastructural changes in lenses seen with microscope; slit lamp picture appeared normal	Williams et al. (1975)
2.45 GHz (CW); single acute exposure of 1.5 kW/m^2, for up to 100 min (SAR peak in vitreous of 138 W/kg, 43 °C peak)	Threshold exposure to produce lens cataract	Guy et al. (1975b)
2.45 GHz (CW); SAR 100 100 W/kg, after > 140 min	Cataract in rabbit	Kramar et al. (1978)
3 GHz (CW); (far-field) 5 kW/m^2, for 30 min	No lenticular changes, periorbital burns	Appleton et al. (1975)
107 GHz or 35 GHz, for 60 min, at 400 W/m^2	Keratitis in cornea; damage more immediate but recovery quicker at 107 GHz	Rosenthal et al. (1976)
Monkeys		
2.45 GHz; 5 kW/m^2, for 60 min	No cataract in rhesus monkey after 13 months	Kramar et al. (1978)

penetration decreases and power absorption becomes increasingly restricted to the superficial tissue (NCRP, 1986).

In general, field intensities associated with the acute induction of cataracts in the rabbit are of such magnitude that they are lethal if applied to the whole animal. Studies on the acute exposure of rabbits' eyes suggest the existence of an RF exposure threshold for the production of a cataract. This is best shown in the data of Kramar et al. (1978) given graphically in Fig. 20. The threshold power density to produce a cataract is approximately 1500 W/m^2 for at least 1 h.

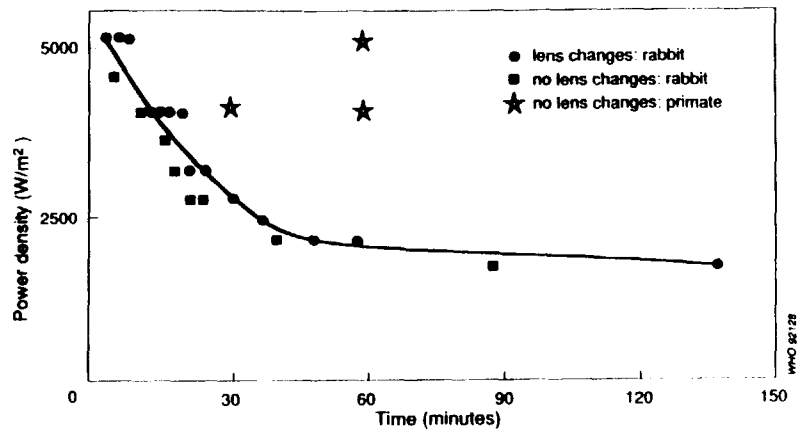

Fig. 20. Threshold for cataract formation in the rabbit exposed to 2.45 GHz microwaves. From: Kramar et al., 1978.

The possibility of a cumulative effect of repeated subthreshold exposure leading to the development of a cataract has been examined, as shown in Table 16. Subthreshold exposures of rabbit eyes caused reversible changes, and damage accumulated only when exposure was repeated before repair had occurred. However, these exposures were only just below the single acute exposure threshold (EPA, 1984). Long-term, whole-body exposures in the far-field at lower levels of power density have not produced any lens opacities.

Opacities were induced in the eyes of anaesthetized primates after exposures well above threshold levels for rabbits, or after long-term exposure of conscious primates (to 9.3 GHz) at up to 1500 W/m^2. It has been suggested that the difference in acute response between rabbits and monkeys reflects structural differences in the face and lens and, hence, energy deposition and heating in the eye.

Table 16. Ocular effects from repeated short-term threshold exposure

Exposure conditions	Effect on exposed group	Reference
Rabbits		
2.45 GHz (CW), at 4.2 kW/m^2	Various degrees of lens opacity :	Carpenter et al. (1960a,b)
4 min for 4 days	- in all rabbits	
4 exposures at 1-week intervals	- in 70% of rabbits	
4 exposures at 2-week intervals	- in 40% of rabbits	
3-min exposure, 5 times in week	- few opacities formed	
3-min exposure, 5 times in 5 weeks	- no opacities formed	
2.45 GHz (CW), at 100 W/m^2 (SAR 1.5 W/kg), for 8 h/day, 5 days/week for 17 weeks	No lens opacities for up to 3 months after exposure	Ferri & Hagan (1976)
2.45 GHz (CW), 1.8 kW/m^2, for 1 h repeated up to 20 times	Cataracts in 8 out of 10 rabbits	Carpenter et al. (1974),
1.5 kW/m^2, for 1 h, repeated up to 32 times	Cataracts in 4 out of 10 rabbits	Carpenter (1979)
1.2 kW/m^2, for 1 h, repeated up to 24 times	Cataracts in 1 out of 9 rabbits	
2.45 GHz (CW), 100 W/m^2 (SAR to head 17 W/kg max), 23 h/day for 180 days	No changes in rabbits eyes	Guy et al. (1980)
Monkeys		
9.3 GHz (CW), 1.5 kW/m^2, 10 h/day for over 3 months	No cataract or corneal lesions found in macaque monkey	McAffee et al. (1979)
2.45 GHz (pulsed-10 μs pulses at 100 Hz), 100 W/m^2, 2.6 W/kg, 4 h/day for 3 days, 2.45 GHz (CW), 200 W/m^2, 6.3 W/kg, 4 h/day for 3 days	Endothelial cell damage to the corneas of monkeys, leakage of iris vasculature; damage greater in timolol maleate-treated eyes	Kues et al. (1985, 1988)
2.45 GHz (10 μs pulses at 100 Hz), 0-100 W/m^2, 4 h/day for 3 days	Leakage of iris vasculature in timolol maleate-treated eyes of anaesthetized adult rhesus and cynomolgus monkeys; damage observed at 10 W/m^2, but not at 2 W/m^2	Monahan et al. (1988)

Histological evaluation of the irises of monkeys, exposed *in vivo*, long-term to 100 W/m^2 pulsed 2.45 GHz at an SAR to the eye of 2.6 W/kg, indicated an increased vascular leakage (Kues et al., 1988). The leakage was increased in exposed animals whose eyes were pretreated with the ophthalmic drug timolol maleate (timolol maleate is used by people with glaucoma to lower the intraocular pressure by reducing the production of aqueous humour). In an extension of this study, Monahan et al. (1988) observed vascular leakage in timolol maleate-treated monkey eyes at power densities as low as 10 W/m^2 (an SAR of only 0.26 W/kg).

The authors suggested that serum protein leakage could have contributed to the corneal endothelial lesions observed in an earlier paper (Kues et al., 1985). More recently, the authors briefly reported that exposure to 50 or 100 W/m^2 pulsed 2.45 GHz over a 10-week period resulted in degenerative changes in the retinal layer (Kues & McLeod, 1990). Timolol maleatic pretreatment increased the severity of the responses. Although requiring further study, these results, if established, could have important implications for the development of standards.

7.3.3 *Auditory perception*

Auditory perception of pulsed RF exposure by animals is well established (see Table 17). For short pulses, thresholds are dependent on the energy density per pulse (Guy et al., 1975a, Chou et al., 1985) rather than the average power density, indicating a thermoelastic interaction.

Table 17. Perception

Exposure conditions	Effect on exposed group	Reference
918 MHz (10 μs pulses at 10 Hz), peak SAR 75 W/kg	Pulsed RF produced similar auditory stimulus for rat behavioural response as a 7.5 kHz tone repeated at 10 Hz	Johnson et al. (1977)
2.45 GHz, pulses with width less than 30 μs	Threshold auditory perception of pulsed RF fields	Guy et al. (1975a)
10-16 mJ/kg:	for cats	Chou et al. (1985)
0.9-1.8 mJ/kg:	for rats	
2.45 GHz (CW), 0.6-2.4 W/kg, for 1 min	Threshold for perception of the RF field in rats	King et al. (1971)

Threshold specific energy densities for pulses shorter than 30 μs were reported as 10-16 mJ/kg for cats and 0.9-1.8 mJ/kg for rats. CW fields are ineffective in generating the rapid thermoelastic expansion necessary for this effect, but can be perceived if temperature sensors in the skin are stimulated; the perception threshold has been reported to lie around 0.6-2.4 W/kg (King et al., 1971).

7.3.4 Behaviour

7.3.4.1 Thermoregulation

Exposure to thermally significant levels of RF will induce a heat load in addition to metabolic heat production (and other sources of heat) and will elicit the various physiological and behavioural mechanisms animals use to regulate body temperature. The thresholds for such responses, given in Table 18, are dependent on the relationships between the total heat load, heat-loss mechanisms, which depend on ambient conditions, and small changes in heat storage. In cool environments, animals compensate for RF-induced body heating by lowering their rate of metabolic heat production. The threshold response of squirrel monkeys, exposed for 10-15 minutes to 2.45 GHz, varied between about 0.5 and 5 W/kg, depending on ambient temperature. Food intake is also reduced in proportion to SAR in animals exposed long-term to RF; a threshold response for rats occurs at around 2-3 W/kg.

Other thermoregulatory responses to RF heating include vasodilation, which increases skin thermal conductance, and sweating. Thresholds of between about 0.3 and 3 W/kg have been described in rats and monkeys. Similar responses have been reported in mice (Stern et al., 1979). Thresholds for behavioural thermoregulation, in which animals selected cooler environmental temperatures or selected shorter durations of infrared heating in response to microwave radiation of around 1 W/kg, have been described in rats and monkeys. Mice were shown to select a cooler environment by moving along a temperature gradient above a threshold SAR of 7 W/kg (Gordon, 1983). The threshold SAR necessary to activate a given thermoregulatory response or raise body temperature varied inversely with body mass (Gordon 1987). Thus, SAR dose-response data must be interpreted carefully when considering the extrapolation from experimental animals to humans.

Table 18. Thermoregulation

Exposure conditions	Effect on exposed group	Reference
Heat production/food intake		
2.45 GHz (CW)	Reduce endogenous heat production to compensate for RF body heating by rats	Ho & Edwards (1977); Phillips et al. (1975)
2.45 GHz (CW), up to 1.5 W/kg	Threshold RF exposure to reduce squirrel monkey metabolic heat production 0.6-0.9 W/kg	Adair & Adams (1982)
2.45 GHz (CW), 0.7 W/kg, 7 h/day for 98 days	No change in food or water intake or weight in rats	D'Andrea et al. (1986b)
915 MHz (CW) - up to 2 W/kg - at 3.2 W/kg	Food intake by rats - not reduced - decreased consumption	Lovely et al. (1977, 1983)
918 MHz (CW), 3.6 W/kg,	Decreased food consumption, but no change in water intake or body weight in rats	Moe et al. (1976)
Vasomotor/behavioural regulation		
2.45 GHz (CW), 5-min sessions, 1 W/kg	Threshold for detectable changes in thermal conductance of skin in squirrel monkeys; power density to cause vasodilation related to ambient temperature	Adair & Adams (1980a)
225 MHz (CW), 1.4 W/kg	Threshold for metabolic and vasomotor responses in rhesus monkeys	Lotz & Saxton (1987)
2.45 GHz (CW), 1.2 W/kg (ambient temperature of 36 °C)	Threshold for sweat response from foot in squirrel monkeys; increased threshold with decreased ambient temperature	Adair (1983b)
2.45 GHz (CW), 10-220 W/m^2, for 10 min	Threshold of approx. 1.2 W/kg for initiation of thermoregulatory behaviour in squirrel monkeys	Adair & Adams (1980b)
450 MHz (CW), for 10-180 min	Threshold of approx. 1.2 W/kg for initiation of thermoregulatory behaviour in squirrel monkeys	Adair & Adams (1988)

Table 18 (*continued*)

Exposure conditions	Effect on exposed group	Reference
2.45 GHz (CW), 1 W/kg	Threshold for initiation of thermoregulatory behaviour in rats	Stern et al. (1979)
2.45 GHz (CW) at 7 W/kg in waveguide with temperature gradient	Threshold for movement from preferred normal ambient temperature	Gordon (1983)
225 MHz (CW), for 6 x 10-min exposure or 120-min exposure, 12-100 W/m^2, 0.35-2.85 W/kg	Heat poorly dissipated by rhesus monkeys at 255 MHz compared with 1.29 GHz	Lotz & Saxton (1988)
1.2 GHz 20 W/m^2 (CW): 2 W/m^2 (pulsed):	Rats: No avoidance of RF field Avoided RF fields	Frey & Feld (1975)

The thermoregulatory responses elicited by RF exposure have been reviewed by Adair, 1988. They were found to be similar to those elicited by exposure to conventional radiant or conductive heat sources. However, the overall thermoregulatory response of an animal to RF exposure will depend on the distribution of RF energy absorption and, thus, on the RF frequency. At frequencies below about 10 GHz, RF radiation is more deeply penetrating than, for example, infrared radiation, and is thus less effective in stimulating the superficial temperature sensitive receptors involved in local (and whole-body) thermoregulatory responses (Adair, 1983a).

The effects of the distribution of RF absorption on thermoregulatory efficacy is particularly marked during exposure at frequencies near whole-body resonance. For example, although qualitatively similar, the thermoregulatory responses of squirrel and rhesus monkeys were less effective in preventing a rise in skin and body temperatures during exposure at resonance than during exposure at supra-resonant frequencies (Adair & Adams, 1988; Lotz & Saxton, 1988).

7.3.4.2 *Activity (spontaneous movement)*

Acute and long-term exposure of rats has been reported to reduce their spontaneous locomotor activity (e.g., Moe et al., 1976, Mitchell

et al., 1988). The rats reduced activity to lower their endogenous heat production. In a lifetime study, activity levels were also reduced after 6 weeks continuous exposure of young rats at up to 0.4 W/kg, but values returned to control levels during subsequent exposure. No other effects on open-field behaviour were reported during 25 months exposure. Table 19 includes a summary of reports on the activity of RF-exposed rats.

7.3.4.3 *Learned behaviours*

Operant techniques that require behavioural responses, such as certain rates of lever pressing in response to a visual or auditory cue, provide a means of assessing the performance of specific learned tasks in a highly quantified and standardized manner. Such studies are summarized in Table 20. It is important to note, however, that threshold values for changes in behaviour will depend on many factors, such as the complexity of the task being performed. To quote single threshold values for a range of tasks is an oversimplification.

In rodents acutely exposed to RF, thresholds for the disruption of operant behaviour have been reported to lie between 2.5 and 8 W/kg, with concomitant rises in rectal temperature of around 1 °C. Deficits in performance have been reported following long-term exposure to 2.45 GHz at 2.3 W/kg. The acquisition of a learned task by rats appears more sensitive to disruption than performance. Thresholds have been estimated of between 0.14 and 0.7 W/kg for long-term exposure to continuous wave RF at 2.45 GHz and between 0.7 and 1.7 W/kg for acute exposure to pulsed 2.8 GHz RF. Auditory effects were avoided by testing after the exposure; however, the data were sometimes variable.

The responses of primates have been less extensively investigated. Operant task performance by rhesus and squirrel monkeys has been reduced by acute exposure to above resonant frequencies (1.3-5.8 GHz) at SARs of between 4 and 5 W/kg. Exposure of rhesus monkeys at whole-body resonance (225 MHz) resulted in reduced task performance at only 2.5 W/kg. However, both thresholds corresponded to raised body temperatures of about 1 °C; the lower threshold for body resonance presumably reflected the deeper heating and less efficient thermoregulation noted in the previous section.

The effects of drugs on behaviour were augmented after pulsed-wave RF exposures of 30 min at an average SAR of 0.2 W/kg (Thomas et al., 1979).

Table 19. Effects on behaviour - activity

Exposure conditions	Effect on exposed group	Reference
2.45 GHz (pulsed), 6.3 W/kg, for 30 min	No differences in the activity of rats	Hunt et al. (1975)
2.45 GHz (CW), 2.7 W/kg, for 7 h	Rats less responsive to novel acoustic stimuli, no effect on acquisition or retention of passive avoidance task, reduced locomotion and rearing	Mitchell et al. (1988)
918 MHz (CW), 3.6-4.2 W/kg, 10 h/night for 21 nights	Lower activity and different temporal distribution of activity of rats	Moe et al. (1976)
2.45 GHz (CW), 1.2 W/kg, 8 h/day, 5 days/week, for 16 weeks	Reduced activity of rats after exposure, but locomotor measures unaffected over long term	D'Andrea et al. (1979)
3 or 10.7 GHz (CW), up to approx. 0.3 W/kg, for 185 h continuously	Activity and stereotypic behaviour (rearing, sniffing etc.) of rats unaffected by RF exposure	Roberti et al. (1975)
2.45 GHz (CW), 7 h/day for up to 14 weeks, 0.7 W/kg intermittent exposures (25 W/m^2)	Decreased activity in rats 30 days after exposure, increased sensitivity to mild AC shock	D'Andrea et al. (1986b)
2.45 GHz (10 μs pulses at Hz, square wave-modulated at 8 Hz), up to 0.4 W/kg, from 2 to 27 months continuous exposure	Except for first session when general activity reduced, no difference in behavioural responses to lifetime exposure of rats	Guy et al. square (1985); Johnson et al. (1983)

Table 20. Effects on behaviour - operant performance

Exposure conditions	Effect on exposed group	Reference
Rats		
2.45 GHz (CW), 0.14 W/kg, 7 h/day, for up to 14 weeks 5 W/m^2	Variable changes in rate of acquisition of operant tasks, not confirmed by DeWitt et al. (1987)	D'Andrea et al. (1986a); DeWitt et al. (1987)
2.45 GHz (CW), 2.5-8 W/kg, for 60 min	Threshold for performance disruption in exposed rats	Sanza & de Lorge (1977); de Lorge & Ezell (1980)
360, 480, 500 MHz (CW), >4 W/kg 250 W/m^2, for up to 25 min	Threshold for reduced performance in rats; rectal temp rise >1 °C	D'Andrea et al. (1976)
600 MHz (CW), >6 W/kg, for up to 55 min	Threshold to stop pressing level for food	D'Andrea et al. (1977)
2.45 GHz (CW), 2.3 W/kg (mean) for 110, 5-h sessions over 22 weeks	Impaired operant performance in exposed rats	Mitchell et al. (1977)
2.37 MHz (CW), 10 or 50 W/m^2, 7 h/day, for up to 90 days	After 10 days exposure, increased learning of avoidance task; up to 90 days decreased retention and reacquisition	Shandala et al. (1977)
2.45 GHz (CW) at 100, 150, or 200 W/m^2, for 15 h (SAR 3, 4.5, or 6 W/kg) or 300 W/m^2 for 55 min (ambient temperature, 22 °C)	Reduced performance fixed ratio alternating operant schedule by rats	Gage (1979a)
2.45 GHz (CW) at 50, 100, 150 W/m^2 for 15 h (SAR 1, 2 or 3 W/kg). (ambient temperature, 28 °C)	Reduced performance random interval operant schedule by rats	Gage (1979b)
2.45 GHz (pulsed, 1 μs pulses at 500 pps), 2-6 W/kg, for 30 min	Impaired performance on discrimination tasks	Thomas et al. (1976)
2.8 GHz (pulsed, 2 μs pulses at 500 pps), 1.7 W/kg, for 30 min	Threshold for decreased acquisition of response sequence schedule	Schrot et al. (1980)

Table 20 (continued)

Exposure conditions	Effect on exposed group	Reference
Monkeys		
2.45 GHz (CW), 5 W/kg, for up to 2 h	Reduced performance and increased response time, rectal temperature increased by 2 °C in rhesus monkeys	de Lorge (1976)
2.45 GHz (CW), > 2.75 W/kg, for 60 min	Reduced performance of observing task in squirrel monkeys; correlated with rectal temperature increase	de Lorge (1979)
225 MHz (CW) 2.5 W/kg or 1.3 or 5.8 GHz (pulsed) 4-5 W/kg	Threshold for impairing performance of observing-response tasks; rectal temperature rise >1 °C in rhesus monkey	de Lorge (1984)
1.2 GHz (CW), 1.6 W/kg repeated 120-min exposures of head	Performance of visual tracking task by rhesus monkey unaffected	Scholl & Allen (1979)

7.3.5 *Endocrine system*

An extensive literature describes the endocrine responses of various species to RF exposure (Table 21). The endocrine responses to acute RF exposure are generally consistent with the acute responses to non-specific stressors, such as heat, or with changes in metabolism caused by hyperthermia (Roberts et al., 1986).

It has been reported in several papers that plasma corticosterone levels in rats were significantly enhanced by exposure above a threshold level that decreased with increasing duration of exposure. Similar effects were found in cortisol levels in primates. The response seems to be modulated in amplitude by the circadian rhythm of cortisol (or corticosterone) levels.

Stressful stimuli are known to depress circulating plasma levels of growth hormone and thyroxin hormones in rodents. Plasma levels of these hormones have been similarly reduced by whole-body exposure of rats to RF. In one study, a threshold response for changes in serum growth hormone levels was reported to be as low as 0.2 W/kg. In contrast, no significant effects on growth hormone or thyroxin levels has been seen in primates.

No effects on the endocrine system were seen in a lifetime study on rats exposed from 2 up to 27 months of age at SARs of up to 0.4 W/kg.

Table 21. Endocrine system effects

Exposure conditions	Effect on exposed group	Reference
Corticosterone/cortisol		
Rats		
2.45 GHz (CW); 500 W/m^2, up to 10 W/kg, for up to 60 min or 200 W/m^2, 3.2 W/kg, for 120 min	Threshold for significant increase in plasma corticosterone levels; Increased (0.7-1.5 °C) colon temperature needed for effect	Lotz & Michaelson (1978)
2.45 GHz (CW), 600 W/m^2, 9.6 W/kg, for 60 min, or 500 W/m^2, 8.3 W/kg, for 60 min for drug-injected rats	Plasma corticosterone levels not increased in hypophysectomized rats or rats injected with dexamethasone (suppresses ACTH release)	Lotz & Michaelson (1979)
2.45 GHz (CW), 100 W/m^2, approx 2.5 W/kg, for 16 h	No change in plasma corticosterone level or rectal temperature	Parker (1973)
2.45 GHz (CW), up to 400 W/m^2, up to 8.4 W/kg for 4 or 8 h	Alteration in normal circadian elevation in corticosterone levels	Lu et al. (1981)
918 MHz (CW), 100 W/m^2, up to 4.2 W/kg, 10 h/day, for 21 days	No change in rectal temperature or in basal or ether stress-induced serum corticosterone levels	Moe et al. (1976)
918 MHz (CW); 25 W/m^2, 1 W/kg (ave), 10 h/day, for 91 days	No change in rectal temperature or serum corticosterone levels	Lovely et al. (1977)
Monkeys		
1.29 GHz (pulsed), 3-4 W/kg, for 4 h	Increased serum cortisol levels and increased rectal temperature (0.7-1.6 °C) but no change in serum growth hormone levels or thyroxin in rhesus monkeys	Lotz & Podgorski (1982)

Table 21 (*continued*)

Exposure conditions	Effect on exposed group	Reference
1.29 GHz (pulsed) 380 W/m^2 4.1 W/kg, for 8 h	Increased serum cortisol levels when rhesus monkeys were exposed during day, but no change when exposed at night; rectal temperature rose by similar amount	Lotz (1983)
255 MHz (CW), 50 W/m^2, 3.4 W/kg, for 4 h	No change in serum cortisol level; rectal temperature increase of 1.5-2 °C in rhesus monkeys	Lotz (1985)
Growth/thyroid hormones		
2.45 GHz (CW), 90-360 W/m^2 SAR up to 7.5 W/kg, for 10 150 min	Decrease in serum growth hormone levels in young rats only when exposed to 7.5 W/kg for at least 60 min; colon temperature rose to more than 40 °C	Michaelson et al. (1975)
2.45 GHz (CW), 500 W/m^2, 10.5 W/kg, for 1 h, or 10 W/m^2, 0.2 W/kg for 2 h	Threshold to induce changes in serum growth hormone levels was dependent on baseline growth hormone level in rats at time of exposure; no change in thyroxin level; no effect with exposure > 4 h	Lu et al. (1980b)
2.45 GHz (CW), 58-190 W/kg, for 120 min	Increased thyroxin and tri-iodothyronine secretion when dog thyroid exposed; increased levels proportional to temperature increase	Magin et al. (1977a,b)
2.45 GHz (CW), 200 W/m^2 or higher, 4.2-5 W/kg, for 4 or 8 h	Depressed circulating thyroxin and TSH levels in rats; rectal temperature rose to about 40 °C	Lu et al. (1977, 1980b)
Other		
2.8 GHz (CW), 100 W/m^2, for 6 h/day, 6 days/week for 6 weeks	Increased luteinising hormone, no change in follicle-stimulating or gonadotrophic hormone levels in rats;	Mikolajczyk (1976)

Table 21 (*continued*)

Exposure conditions	Effect on exposed group	Reference
2.45 GHz (pulsed), 4.8 W/m^2, 0.15-0.4 W/kg, continuous exposure of rats from 2 to 27 months of age (lifetime exposure)	no differences in plasma endocrine levels between exposed and control animals	Johnson et al. (1983) Guy et al (1985)

7.3.6 *Haematopoietic and immune systems*

In a large number of studies, haematological effects have been found in animals exposed to RF, mainly when a significant rise in body temperature has been observed. Few effects have been reported in the absence of a detectable increase in temperature, as shown in Table 22. Athermal responses have not been established.

Smialowicz (1984) reviewed earlier studies and did not find any consistent effects of RF exposure on peripheral blood cells in developing rats. No consistent changes were found in erythrocyte, leukocyte, or differential leukocyte cell counts in rats exposed pre- and post-natally to RF fields.

RF exposure has been reported to affect various components of the immune system. Whilst both stimulatory and inhibitory responses have been reported, these have been mostly transient in nature and usually attributable to thermal stress.

Several authors have noted that exposure to thermogenic levels of RF will result in increased levels of circulating neutrophils and decreased levels of circulating lymphocytes (see Fig. 21 from Liburdy (1979) and Table 23). A lack of effect of low-level exposure on circulating blood cell count in rats has been reported in other studies. On the basis of his results, Liburdy (1979, 1980) suggested that whole-body RF exposure induces heat stress that activates the hypothalamic-hypophyseal-adrenal axis to trigger the release of adrenal steroids into the blood, leading to the transient changes in blood cell counts and other haematopoietic and immunological changes associated with RF exposure.

Table 22. Haematopoietic system effects

Exposure conditions	Effect on exposed group	Reference
Circulating blood cells		
800 MHz, 430 W/m^2 (average), 2 h/day, 5 day/week, for 35 weeks, SAR estimated at less than 1.5 W/kg	No change in erythrocyte count, haemocrit, or haemoglobin concentration in mice; 4 exposed mice died	Spalding et al. (1971)
2.95 GHz, 30 W/m^2 (average), for 158 h (CW or pulsed)	Decreased erythrocyte production in rabbits; pulsed exposure more effective	Siekierzynski (1972)
2.4 GHz (CW) 100 W/m^2 for 2 h/day, for up to 30 days, SAR approx 2 W/kg	Increased erythrocyte count; 1 ^{0}C rise in rectal temperature in rats	Djordjevic & Kolak (1973)
26 MHz(CW) SAR 13 W/kg, for up to 3 h; rectal temperature rose by 2-4 °C	Decreased peripheral lymphocytes, increased neutrophils in mice	Liburdy (1977)
2.45 GHz (CW) 300 W/m^2, for 30 min/day for 22 days, SAR 22 W/kg	No effect on peripheral blood cell count in mice	Smialowicz et al. (1979a)
2.4 GHz (CW) 50 W/m^2, 1 h/day for 90 days, SAR approx 1 W/kg	No effect on peripheral blood cell count in rats	Djordjevic et al. (1977)
970 MHz (CW) SAR 2.5 W/kg, 22 h/day for 70 days	No effect on blood count in rats	Smialowicz et al. (1981a)
2.45 GHz (CW) SAR 2.2 W/kg, for 8 h	No effect on peripheral blood cell count in rats	Galvin et al. (1982)
20 MHz (CW) SAR 0.3 W/kg, 6 h/day for up to 6 weeks	No effect on blood cells in rats	Wong et al. (1985)
2.45 GHz (CW), 5 W/kg 100 MHz (CW), 3 W/kg 425 MHz (CW), 7 W/kg	No consistent changes in erythrocyte or leukocyte counts in rats exposed pre- or postnatally, for up to 41 days	Smialowicz et al. (1979b, 1981b, 1982) Smialowicz et al. (1982)

Table 22 (*continued*)

Exposure conditions	Effect on exposed group	Reference
Bone marrow cells		
2.95 GHz (CW) 10 W/m^2, for 4 h/day for 14 days in guinea-pig; 4 h at 5 W/m^2 in mice	Shift in circadian rhythm of division of blast cells in bone marrow and lymphocytes; no statistical analysis, hence, response suggestive only	Czerski et al. (1974a); Czerski (1975)
2.45 GHz (CW), 150 W/m^2 SAR 11 W/kg, 30 min/day for 9 days	Reduced ability of mouse bone marrow cells to form myeloid or erythroid colonies *in vitro*	Huang & Mold (1980)
2.88 GHz (pulsed) SAR 4.5 W/kg, 7.5 h/day for 360 days	Significant but inconsistent alterations in bone marrow, blood cell and serum protein values in mice	Ragan et al. (1983)
General long-term studies		
2.45 GHz (CW), SAR 1.5 W/kg, 23 h/day for 180 days	41 parameters measured, only 3 of which changed; Lower eosinophil, serum albumin, and calcium levels in rabbits	McRee et al. (1980)
2.45 GHz (pulsed) SAR 0.15-0.4 W/kg, for 25 months	No effect on haematology or serum chemistry parameters in rats	Guy et al. (1985)

Exposure to thermogenic levels of RF fields has been shown to cause several effects including a depression of natural killer cell activity, implicated, for example, in tumour cell cytolysis, and macrophage activation. One group of workers (Wiktor-Jedrzejczak et al., 1977a,b, 1980) reported an increase in the number of lymphocytes bearing a surface marker (complement receptor) in mice exposed to high levels of microwave radiation. Smialowicz et al. (1979a) were unable to replicate this effect using a different strain of mouse. This difference in response between the two strains may be due to the presence of a single gene located on chromosome 5 (Schlagel et al., 1980, 1982). At present, this remains an unresolved issue.

Table 23. Immune system effects

Exposure conditions	Effect on exposed group	Reference
Mitogen response - blast transformation		
2.45 GHz (CW) SAR 21 W/kg, 15 min/day, for 5 days	Transient increase in transformation rate of peripheral blood lymphocytes (to lymphoblasts) in Chinese hamsters, decreased mitotic frequency in mitogen-stimulated lymphocytes	Huang et al. (1977)
2.45 GHz (CW) up to 150 W/m^2 SAR 11 W/kg, 30 min/day, for 17 days	Altered mitogen response of T- and B- lymphocytes in Balb/c mice	Huang & Mold (1980)
2.45 GHz (CW) up to 300 W/m^2 SAR 22 W/kg, 30 min/day, for 22 days, or 11 W/kg, 1.5 h/day, for 9 days	No effect on mitogen response of T- and B- cells in Balb/c mice or CBA/J mice	Smialowicz et al. (1979a, 1983)
10.5, 19.27, 26.6 MHz (CW) up to 2 W/kg, for 30 min	Enhanced mitogen response in lymphocytes from rhesus monkeys; rectal temperature increased up to 2.5 °C.	Prince et al. (1972)
Surface (complement receptor) marker		
2.45 GHz (CW) up to 15 W/kg, for 30 min	Increased lymphocytes with surface marker (complement receptor) in CBA/J mice	Wiktor-Jedrzejczak et al. (1977a,b,1980)
2.45 GHz (CW) up to 22 W/kg, for 30 min on 22 consecutive days	No increase in complement-receptor positive lymphocytes in Balb/c mice	Smialowicz et al. (1979a)
2.45 GHz (CW) 14 W/kg	Increase in complement-receptor positive lymphocytes in >12-week-old CBA/J mice; no effect in BALB/c mice	Schlagel et al. (1980, 1982)
2.45 GHz (CW) 28 W/kg	Increase in complement-receptor positive lymphocytes in 16-week-old CBA/J mice	Smialowicz et al. (1981c)

Table 23 (*continued*)

Exposure conditions	Effect on exposed group	Reference
Lymphocyte circulation		
26 MHz (CW); 5.6 W/kg, for 15 min (single or repeated) in warm air environment; rectal temperatures rose by 2-3 °C	Reduced mouse peripheral lymphocytes; increased neutrophils, T- and B- cells in spleen, elevated corticosteroid levels	Liburdy (1979)
2.6 GHz (CW), for 1 h	Lymphocyte circulation, lung, spleen, and bone marrow - changes only when rectal temperature of mice increased;	Liburdy (1980)
at 19 W/kg:	Altered significantly;	
at 3.8 W/kg:	Not affected	
Macrophage/NK T-cell activity		
2.45 GHz (CW); SAR 13 W/kg	Activation of macrophages in hamsters (depressed killer T-cell activity)	Rama Rao et al. (1983)
2.45 GHz (CW) for 1 h	Natural killer T-cell activity in hamster: (Changes due to heat stress?)	Yang et al. (1983)
at 13 W/kg, colon temperature >3 °C:	Transient decrease	
at 8 W/kg:	Unchanged	
2.45 GHz (CW); 21 W/kg; Increased rectal temperature	Transient decrease in killer T-cell activity; increased macrophage activity in mice	Smialowicz et al. (1983)
2.45 GHz (CW); 22 W/kg 5 x 30 min; no significant rectal temperature increase	No change in killer T-cell activity in mice; increased macrophage activity	Huang & Mold (1980)
Antibody response		
9 GHz (pulsed); 100 W/m^2 (average) SAR 4.7 W/kg, 2 h/day for 5 days	Stimulation of antibody response and increased survival time of mice injected with pneumococcal polysaccharide	Liddle et al. (1980)

Table 23 (*continued*)

Exposure conditions	Effect on exposed group	Reference
2.375 GHz (CW); 0.1, 0.5, 5.0 W/m^2, for 7 h/day for 45 days	Appearance of circulating *autoantibodies in rats* against brain and liver tissue and antibodies against fetal tissue in pregnant dams only at 5.0 W/m^2	Shandala & Vinogradov (1982, 1990)
As above, except SAR 0.47 W/kg	No effect on normal antibody response and survival	Liddle et al. (1986)
2.45 GHz (CW), for 1 h	*Primary* antibody response of spleen lymphocytes to sheep RBCs in hamsters:	Rama Rao et al. (1985)
8 - 13 W/kg	increased	
< 8 W/kg	no change	
Long-term: Juveniles/adults		
2.45 GHz (CW), up to 5 W/kg, *for up to 41 days* of age	Increased lymphocyte *response to T- and B-* mitogens in rats	Smialowicz et al. (1979b)
425 MHz (CW), up to 7 W/kg, for up to 41 days of age	Same as above	Smialowicz et al. (1982)
100 MHz (CW), SAR 2-3 W/kg, for 4 h/day, until 97 days of age	No effect on blood cell count, mitogen or antibody response in rats	Smialowicz et al. (1981b)
2.45 GHz (10 μs pulses, 800 Hz) 4.5 W/m^2, SAR 0.15-0.4 W/kg, up to 27 months of age	No significant differences in immunological parameters in rats; transient change in lymphocyte count and responsiveness at 13 months	Guy et al. (1985)

The results of studies on the developing immune system, shown in Table 23, may indicate an effect of the higher SARs on lymphocyte responsiveness. This effect is consistent with other reports and with observations of increased lymphocyte activity elicited by conventional heating (Roberts, 1979).

A lifetime exposure study (Guy et al., 1985) in which rats were exposed to up to 0.4 W/kg between 2 and 27 months of age did not reveal any effects on haematological or immunological parameters,

except for a transient change in the number and responsiveness of B- and T-lymphocytes to specific mitogens after 13 months exposure.

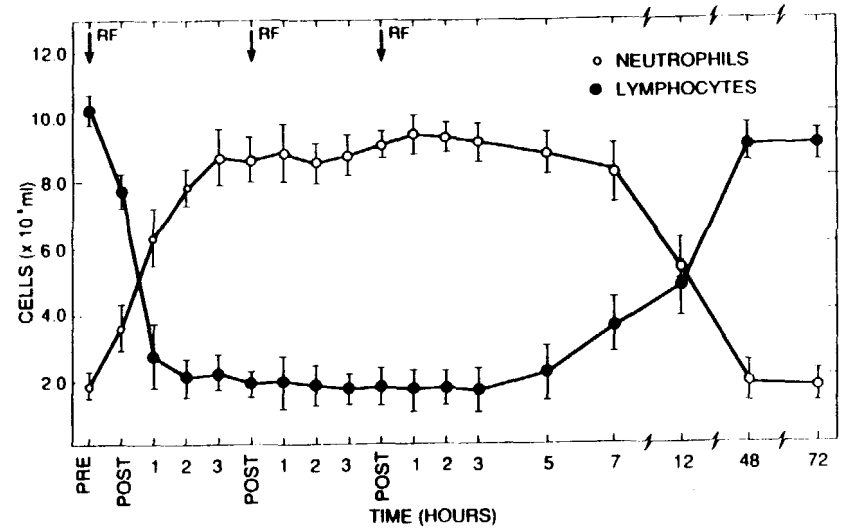

Fig. 21. Changes in neutrophil and lymphocyte counts in mice after repeated exposure to RF fields. "Pre" and "post" indicate counts immediately before and after RF exposure, respectively. Values represent means ± standard deviations. From: Liburdy (1979).

7.3.7 *Cardiovascular system*

The responses of the intact cardiovascular system to exposure to RF, as shown in Table 24, are consistent with those associated with conventional heating. Hence, depending on the ambient temperature, the SAR, and duration of exposure, increases in heart rate (tachycardia), no change, or decreases in heart rate (bradycardia) can be induced during, and following, RF exposure.

Table 24. Cardiovascular system effects

Exposure conditions	Effect on exposed group	Reference
During exposure		
2.45 GHz (CW); 100 W/m^2, SAR 2 W/kg, for 20 min applied to heads	No heart rate effects in rabbits	*Birenbaum* et al.(1975)
2.45 GHz (CW), 50 or 800 W/m^2 or 50 W/m^2 (pulsed) whole-body SAR up to 15 W/kg	Increased heart rate only at 800 W/m^2 in rabbits; normal response to heating	Chou et al. (1980)
2.45 GHz (CW); SAR 2.3 W/kg for 6 h	No effect on arterial blood pressure, but heart rate reduced by 10% in rats	McRee et al. (1988)
4 GHz, CW or amplitude-modulated at 16 Hz (70% mod.), for 30 min, SAR in cortex 8.4, 16.8, or 42 W/kg	Transient bradycardia during CW or modulated RF in anaesthetized rats	Mangel et al. (1990)
After exposure		
2.45 GHz (CW), 30 min to SARs up to 11.1 W/kg in rats; environmental temperature 24 °C	At 6.5 W/kg, mild bradycardia in rats for up to 3 h; at 11.1 W/kg, pronounced bradycardia for 2 h, followed by mild tachycardia and irregular heart rate for short periods; threshold between 4.5 and 6.5 W/kg	Phillips et al. (1975)
915 MHz (CW), SAR 2.5 W/kg, for 8 h/day, 5 days/week, for 16 weeks	No change in heart weight in rats	D'Andrea et al. (1980)
435 MHz (pulsed: 1 μs pulses at 1000 Hz) 10 W/m^2 whole-body SAR approx 0.35 W/kg, for 22 h/day over 6 months	No change in resting heart rate or mean arterial blood pressure in rats	Toler et al. (1988)

An increase in cardiac output, heart rate, and blood pressure, coupled with a decrease in peripheral resistance, has been reported in rabbits exposed at SARs estimated at 10-15 W/kg (raising body temperatures 0.5 °C) and in anaesthetized rats exposed at levels that increased body temperature by about 3.5 °C. Following exposure, heart rate decreased; the threshold for this effect was between 4.5 and 6.5 W/kg. Long-term exposure of rats at SARs of between 0.3 and 2.5 W/kg did not affect heart rate or heart weight.

7.3.8 Reproduction and development

The assessment of the toxic effects of an agent on fertility and the development of the embryo and fetus are of great importance. The processes of meiosis, fertilization and implantation, and the high rates of cell division and differentiation during development of the embryo and fetus tend to be more susceptible to toxic insults than many other processes in the tissues of the adult organism.

7.3.8.1 kHz studies

Studies in the kHz range are summarized in Table 25. The fields used are generally of the type generated by clinical exposure systems or by some types of visual display units. These studies have not shown consistently reproducible effects. Exposure of developing chick embryos to pulsed electromagnetic fields, including a signal of the type used clinically for bone healing, for up to a week, had no effect on malformation incidence (Sisken et al., 1986). Studies of effects on mammals are of greater relevance to human health.

Two teratological studies (Tribukait et al., 1987; Stuchly et al., 1988) on the effects of magnetic fields of the type used in VDUs reported increased numbers of malformed fetuses in rodents, but, when the results were analysed using the litter rather than the individual fetus as the unit of observation, the increases were not significant (Stuchly et al., 1988).

Table 25. Teratological studies in the kHz region

Exposure conditions	Effect on exposed group	Reference
Chicks		
Pulsed magnetic fields 10, 100, or 1000 Hz; up to 1.2 μT, for first 48 h of development	Abnormal development, particularly in cephalic region; effect most marked at 100 Hz	Delgado et al. (1982).

Table 25 (*continued*)

Exposure conditions	Effect on exposed group	Reference
Pulsed electromagnetic fields, 3.8 kHz, 50 ms burst repeated at 2 Hz (0.25 mT peak) or 4.4 kHz, 5 ms burst repeated at 15 Hz (1.6 mT) to embryos for first 24 h or 7 days of development	No significant increase in incidence of abnormalities	Sisken et al. (1986)
20 kHz sawtooth magnetic fields 0.1-16 μT applied to embryos for first 42 or 47 h of development	No effect on incidence of malformation	Sandstrom et al. (1987)
Mammals		
20 kHz sawtooth magnetic fields 1 or 15 μT applied to embryos on days 0-14 of gestation	Significant increase in number of mouse fetuses with external malformations at 15 μT (difference not significant if analysed by litter (Stuchly et al., 1988)	Tribukait et al. (1987)
20 kHz sawtooth magnetic fields 15 μT applied to embryos on days 0-19 of gestation	Increased number of implants and post-implantation deaths in mice; no effect on incidence of malformation	Frolen et al. (1987)
19 kHz sawtooth magnetic fields 5.7, 23, for or 66 μT, for 7 h/day, before and during gestation	No effect on post implantation survival in rats; increase in minor skeletal defects in highest exposure group, but only if analysed by individual fetus and not by litter	Stuchly et al. (1988)

7.3.8.2 *MHz and GHz studies*

(*a*) *Fertility*. Most of the studies on reproduction and development in small mammals exposed to RF radiation have shown effects that can be related to an increase in temperature, and can be produced by thermal stress alone. It is well known that, in many species of mammal, the development of male germ cells can be adversely affected by increased testicular temperatures. The studies shown in Table 26 indicate that acute RF exposure of anaesthetized animals can, through raising testicular temperature, affect the spermatogenic

Table 26. Effects on male fertility

Exposure conditions	Effect on exposed group	Reference
Anaesthetized		
2.45 GHz (CW), or direct heating of lower half of body, for 30 min	Depletion of primary spermatocytes and spermatids in mice; threshold temperature for depletion 39 °C or SAR of 30 W/kg or greater; increased number of abnormal sperm at higher temperatures	Saunders & Kowalczuk (1981); Kowalczuk et al. (1983)
1.3 GHz (pulsed), 8-10 W/kg, for 60 min or more	Depletion of primary spermatocytes and spermatids in rats; threshold temperature 39-41 °C	Lebovitz et al. (1987)
Conscious		
2.45 GHz (CW), up to 20 W/kg, 16 h/day, for up to 30 days	No effect on sperm count or number of abnormal sperm in conscious mice	Cairnie & Harding (1981)
2.45 GHz (CW), 5 W/kg, for 120 h over 8 weeks, then mice mated over next 8 weeks	No effect on conscious, male mouse fertility, pregnancy rates	Saunders et al.(1988)
2.45 GHz (CW), 5.6 W/kg, for 80 h over 4 weeks	Transient reduction in conscious, male rat fertility, 50% of dams mated 3-9 days after irradiation of males showed pregnancies; rectal temperature 41 °C	Berman et al. (1980)
1.3 GHz (pulsed), 6.3 W/kg, 6 h/day for 9 days	No effect on sperm production, sperm morphology, testes mass, etc. in rats; body temperature rise of 1.5 °C; no effect on different stages of spermatogenesis, except for a reduction in heat sensitive pachytene spermatocytes	Lebovitz & Johnson (1983); Johnson et al. (1984)
1.3 GHz (CW), 9 W/kg, for 8 h, rectal temperature rise 4.5 °C	No differences in testicular function of conscious rats	Lebovitz & Johnson (1987)