from activity of adjacent cells or as tissue components of environmental EM fields, Adey (1993).

A schematic of the cell plasma membrane is given in Figure 20, from Bretscher (1985).

These stranded protein molecules are the structures providing signal transduction of biochemical messages into the cell to alter cell metabolism or behaviour as a response to external (cell to cell, or environmentally sourced) stimuli.

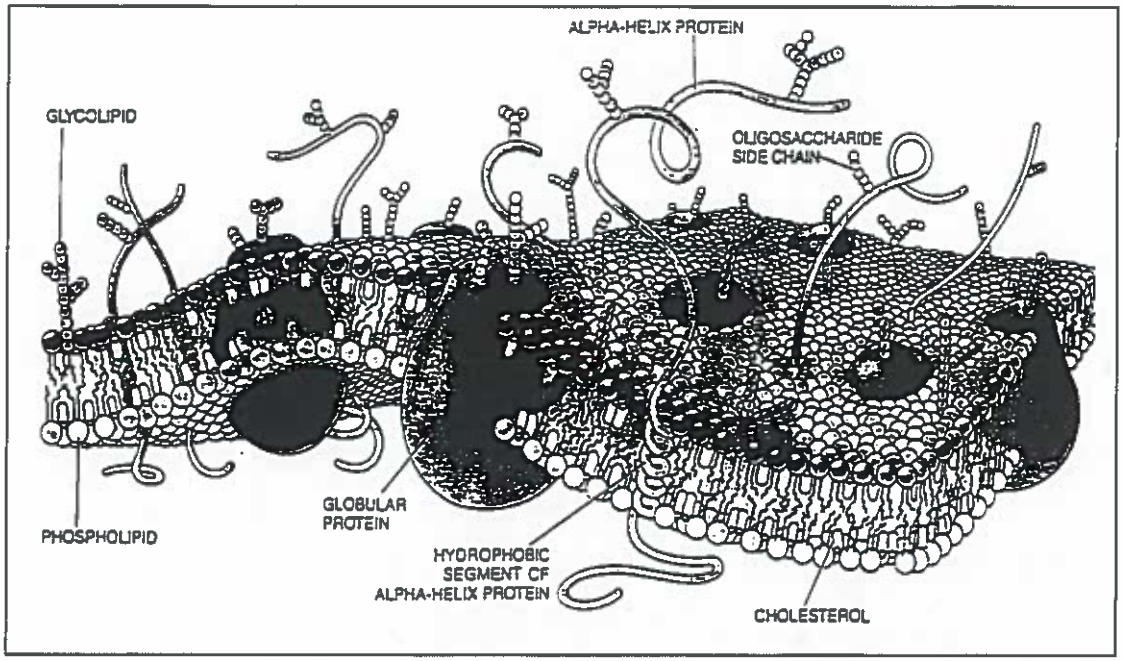

Figure 20: Cell membrane (schematic) showing the bimolecular layer in which cholesterol and other protein molecules are imbedded, with the stranded (alpha-helix) protein which has a coiled hydrophobic section within the membrane and "Y" shaped receptor sites on the extracellular strands, Bretscher (1985).

The amino acid sequence of these stranded proteins reveals a hygrophobic segment of 23 amino acids in the portion which passes through the cell membrane, and the response of these strands to epidermal growth factor (EGF) results in the proposition that this short segment produces vibration modes in the helical proteins which act as a nonlinear amplifier of the signal, Ullrich et al. (1985), Lawrence and Adey (1982).

11.6 Signal transduction messengers:

An external signal (first messenger) is provided by a messenger binding to a receptor on the stranded protein. The alpha helix transfers the message by changing shape successively down its length. At some point the signal is transferred to ions or chemicals in the cytoplasm through the action of an "amplifier" enzyme. A typical amplifier process involves adenylate cyclase which converts adenosine triphosphate (ATP) to cyclic adenosine monophosphate (AMP) (cAMP) by removing two of the three phosphate groups. ATP serves the cell by donating energy to chemical reactions. The intracellular signals are carried by "second messengers" such as cAMP.

The number of second messengers is surprisingly small, in other words, the intracellular signal pathways are remarkably universal. Yet the known messengers are capable of regulating a vast variety of physiological and biochemical processes.

Three of the major signal pathways are:

1. The Adenylate cyclase pathway, converting ATP to cAMP, both enhanced by stimulation and reduced by inhibition. This also modifies the calcium pathway.

2. The calcium ion, IP_3 and DG, pathway. This plays a central role in the regulation of cell growth and is not known to be inhibited.

3. The polyamine pathway, which involves the enzyme ornithine decarboxylase (ODC).

Figure 21 shows a schematic of the first two of these signal transduction pathways.

The third signal transduction pathway involves polyamine biosynthesis. The polyamines are found ubiquitously in nature and have been closely linked to the processes of cell proliferation, hypertrophy and differentiation in eukaryotic cells, Byus (1994). (Eukaryotic cells are cells of higher plant and animals, having a true nucleus). ODC decarboxylates, or removes, the carboxyl group from ornithine to yield putrecine or diainobutane, and by a further series of reaction yields spermidine and spermine, Byus (1994). Enhancement of Ornithine decarboxylase (ODC), the key regulatory enzyme in mammalian polyamine biosynthesis, is rapidly induced by mitogens and tumor promoters, Mar et al. (1995).

Elevated levels of ODC have been found in a number of animal and human tumours, for example stomach, colon and esophagus, Yoshida et al. (1992). A detailed analysis of ODC in Human Colon Cancer suggests that ODC activity is influenced by kinase activity, with protein kinase C being the most likely candidate, Sumiyoshi et al. (1991). Mustelin et al. (1987) have shown that ODC is also linked to T-cells membrane so that activation of ODC can be linked to neoplastic changes in cells and to alteration of immune system cells.

Due to the high sensitivity of this enzyme (ODC) to a large variety of stimuli and the involvement of changes in ODC activity and polyamines in a variety of pathologies, including cancer, ODC appeared to be a logical choice to investigate as a potential marker of exposure of cells or tissues to low-energy electromagnetic fields, Byus (1994).

Given the fundamental role of the signal transduction processes in the regulation and control of cell processes, including proliferation which occurs in cancer cells, and in the development of all cells in human bodies including brain, CNS and immune system, any evidence of changes in these processes because of exposure to environmental electromagnetic radiation is of grave concern.

The research reported below documents many induced changes at the cellular level due to EMR exposure. This follows with epidemiology showing increased health risks associated with increased EMR exposure.

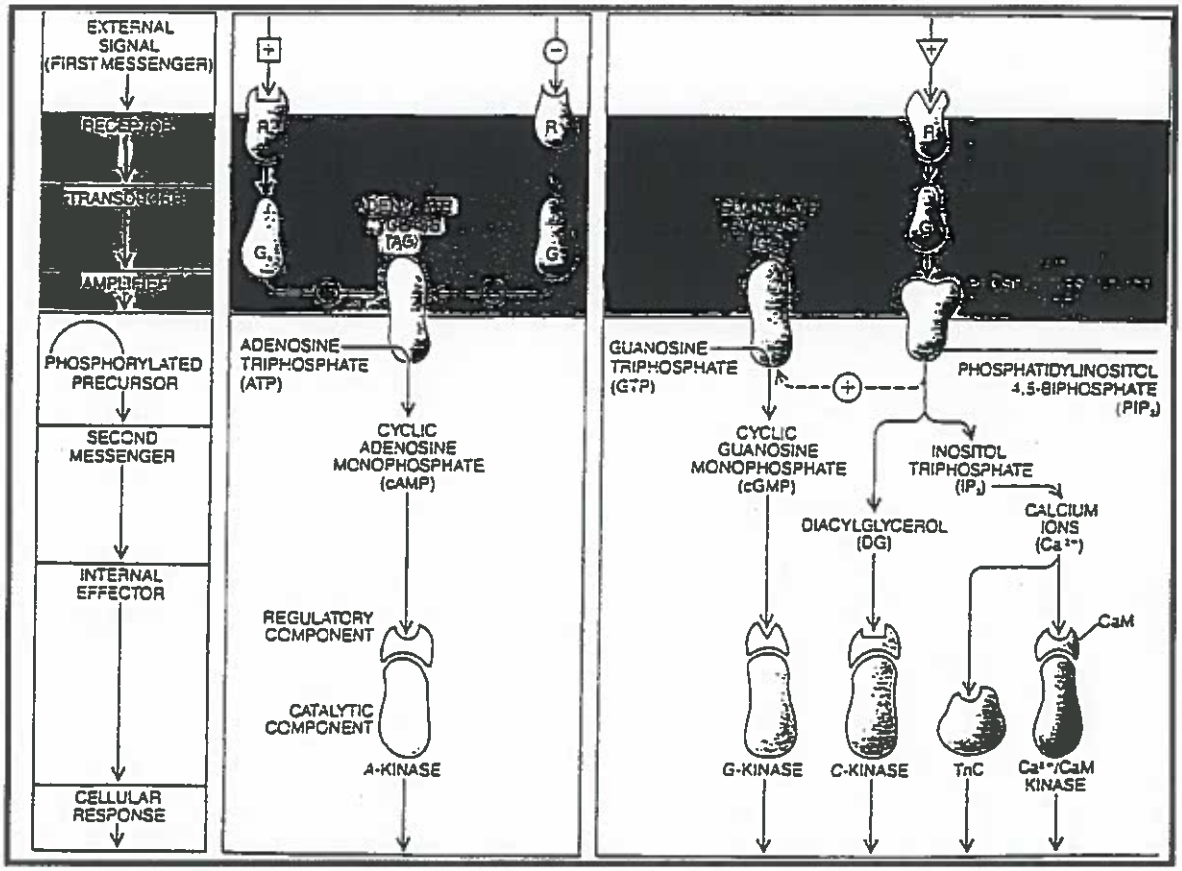

Figure 21: Schematic of two of the signal transduction pathways, with the general scheme on the left, the cAMP pathways in the center and the DG/IP_3/Ca^{2+} pathway on the right, Bretscher (1985).

11.7 Signal Transduction Alteration by EMR:

Many laboratories have now observed increases in the enzyme ODC in cultured cells following a variety of electromagnetic fields, from pulsed static and ELF fields to modulated microwave fields. At least six separate laboratories have observed changes in ODC activity comparable to what is reported here when monolayer cultured cells were exposed to a number of ELF exposure paradigms, including pulsed electromagnetic fields, 50 Hz amplitude modulated 450 MHz fields, and 50-65 Hz electromagnetic fields, Byus (1994).

Luben (1995) summarizes the concept of signal transduction in cells and the effect of EMR:

"Clearly, any environmental influence (e.g. electromagnetic fields) that modifies signal transduction pathways in normal cells could also influence the potentially tumorigenic pathways in susceptible cells, either by enhancing the likelihood of transformation by other tumorigenic stimuli of by acting in a direct tumorigenic manner. Thus, it is not necessary to hypothesize, as some have done, that EMF must cause genetic damage to cells in order to cause cancer or developmental abnormalities. Nor is it necessary to hypothesize that EMF must alter the expression of genes in

cells directly (indeed, recent studies make this hypothesis seem rather unlikely).

By influencing signal transduction pathways, which in turn can generate cell proliferation, cell differentiation, and even transformation to a cancer phenotype, EMF can potentially be involved in a host of disease processes without ever penetrating the cell membrane in any significant manner."

There is clear biological evidence at the cellular and molecular level which shows that RF/MW radiation can be absorbed at very low levels and produce significant changes in cell behaviour and structure through signal transduction, including carcinogenic activity. Galvanovskis et al. (1996) show that modulated EMR fields change the concentrations of calcium ions and their oscillations in human leukaemia T-cells. T lymphocytes (T-cells) recognize intracellular antigens, presented at the surface of the cells. Thus there are biological mechanisms which could be related to the production of childhood leukaemia as identified through epidemiology.

11.8 Alterations in Ornithine Decarboxylase activity:

Being a frequency-related effect, the degree of coherence of the ELF signal or the modulation frequency can be relevant. Litovitz et al. (1993) investigated this matter using L929 mouse fibroblast cells exposed to 915 MHz microwaves modulated at 55, 60 and 65 Hz, with an SAR of 2.5 W/kg. They found that, as for ELF signals, a period of coherence of about 10 s was required to gain the full ODC enhancement. Litovitz et al. (1994), using a 60 Hz signal, imposed noise containing frequencies from 30 to 90 Hz.

They determined that full ODC enhancement was obtained when the rms value of the noise was less than one tenth of that of the coherent signal. These results could well have been influenced by the thermal noise of the rather intense microwave signal used. Referring back to table 2, no effect was found for calcium-ion efflux at 0.2 W/kg and higher but very significant effects were found between 0.00015 and 0.075 W/kg.

Byus et al. (1987) investigated the ODC activity in a number of established cell lines under the influence of low-energy 60 Hz EM fields. They used a 1 hr exposure to a 10 mV/cm 60 Hz field which produced a 5-fold increase in ODC activity in human lymphoma CEM cells and a 2- to 3-fold increase in mouse myeloma cells (P3) relative to unexposed cultures. Depending on the cell type, the ODC activity remain elevated for several hours after the 1 hr exposure had ceased. Reuber H35 hepatoma cells grown in monolayer culture had a 30 % increase in ODC activity with a 0.1 mV/cm field applied for 1 hr, but no effect from a 10 mV/m field applied for 2 or 3 hrs. This is another example where high intensities find no change but lower intensities do cause biological changes. Hence, while results vary with exposure interval and field strength, this shows that EMR alters ODC activity in such a way that 60 Hz fields are shown to have the potential ability as a tumour promoting stimulus in the same way that ELF modulated RF/MW also does.

Note, all the experiments reported by Byus et al. (1987) were carried out at 60 Hz and no other frequencies were investigated.

Byus et al. (1988) showed a 50 % increase in ODC activity in Reuber H35 hepatoma cells with 450 MHz microwaves modulated at 16 Hz for 1 h. This was an athermal exposure,

giving less than 0.1°C temperature rise, with a 1 mW/cm^2 peak-envelope-power and an SAR of 0.08 W/kg. With σ=1.2 S/m, Eq. 11 estimates the exposure as S=35 μW/cm^2. The effect persisted for several hours following exposure. Modulation frequencies of 60 Hz and 100 Hz had no effect. A phorbol ester tumour promoter (TPA) enhanced the ODC activity in combination with the EMR. Similar ODC activity changes were observed when Chinese Hamster ovary cells and 294T melanoma cells were exposed to the radiofrequency EMR regime.

While the mechanism by which EM fields increase ODC activity is still unknown, from the observation that brief exposure of cells to EM fields altered the cell's responsiveness to TPA, and the fact that TPA has a specific receptor in the membranes of all cells, this suggests that this, and other data, are consistent with the concept that protein kinase C in the membrane may be a target for low energy EM fields.

The observation, Balcer-Kubiczek and Harrison (1985), that prior exposure to microwaves (2.45 GHz, 130 pps) led to the enhanced effect of benzpyrene- or X-ray-induced transformation frequencies, provided the cells were treated with TPA, is also consistent with the hypothesis that primary cellular effects of low level microwave fields and of TPA, is at the level of the cell membrane.

Balcer-Kubiczek and Harrison (1985) conclude that this is further evidence that microwaves are cancer promoters using mechanisms which are athermal and act at the cell membrane level. Direct application of this to animal and human cancer is found in Sumiyoshi et at. (1991). They state:

> **"ODC is a rate-limiting enzyme in the biosynthesis of polyamines linked with normal and neoplastic cell proliferation. Induction of ODC has been suggested to play an important role in tumor including skin, urinary bladder, stomach and colon carcinogenesis in rodent models. ...**
>
> **Studies have shown that human colonic mucosal levels of ODC activity are lowest in colonic mucosa from healthy controls but are increased in normal-appearing mucosa from subjects with colonic polyps and from colon cancer patients."**

Yoshida et al. (1992) , investigating levels of ODC gene in human cancers, found that the ratios of ODC mRNA in tumours compared to normal tissue was 14.6 ± 3.7 for all

esophageal cancers, 2.9 ± 0.9 for stomach cancer, 2.1 ± 0.9 for colon cancers, and 0.9 ± 0.2 for liver tumours.

11.9 ODC Summary and Conclusions:

Research shows that ODC, a growth regulating enzyme in the polyamine signal transduction pathway, is enhanced in a number of cell lines, including human cells, in the presence of ELF or ELF modulated RF/MW radiation. The mechanism is at yet unknown but could well involve protein kinase C in a receptor on the surface of the cell membrane.

This is relevant to the effects of signal transduction pathways on the formation and promotion of cancer for it is found that ODC levels are highly elevated in neoplastic tissue in many human cancers. The relationships between signal transduction processes, cell growth, differentiation and neoplastic transformation of cells is very complex.

What is relevant here is that many genes known to be oncogenes are clearly analogous to membrane receptors or to molecules involved in the signal transduction pathways activated by membrane receptors. Intracellular regulatory pathways such as the cell division cycle and the promotion of differentiation and gene expression are very likely to be modulated by a multitude of signal transduction pathways in both normal cells and in neoplastically transformed cells, Luben (1995).

Clearly, any environmental influence, such as electromagnetic fields, that modifies signal transduction pathways in normal cells could also influence the potentially tumorigenic pathways in susceptible cells, either by enhancing the likelihood of transformation by other tumorigenic stimuli or by acting in a direct tumorigenic manner.

Thus it is not necessary to hypothesize, as some have done, that EMF must cause genetic damage directly to cells in order to cause cancer or developmental abnormalities. Nor is it necessary to hypothesize that EMF must alter the expression of genes in cells directly. By influencing the signal transduction pathways, which in turn can regulate cell proliferation, cell differentiation and even transformation to a cancer phenotype, EMF can potentially be involved in a host of disease processes without ever penetrating the cell membrane in any significant manner, Luben (1995).

12. Calcium Ions:

12.1 Calcium Ion Processes:

12.1.1 Ionic calcium is ubiquitous in mammalian cells.

Calcium is nearly ubiquitous in human cells. Calcium ions (Ca^{2+}) play vital rolls in many biological processes of living tissues, including signal transduction processes at the cell level, which includes processes which control the binding and release of molecules to the surfaces of cells which influence primary cellular behaviour. The intracellular fluid (fluid inside the cell membrane surrounding the cellular nucleus), is rich in calcium ions. When calcium ions flow outwards through the cell membrane, it is called "calcium-ion efflux".

A molecular analysis of the cAMP pathway shows that cAMP often activates the calcium ion pathway and modulates its activity. The heart provides a now classic example. There epinephrine acts through the cyclic AMP pathway to modulate the level of

intracellular calcium. This the force of each heart beat which is governed by a brief calcium pulse.

In certain cells, such as neurons, the source of calcium ions is well known: it is the extracellular fluid. Nerve signals arriving at the synaptic terminals of a neuron decrease the voltage across the neuronal cell membrane; the resulting "depolarization" opens voltage-sensitive calcium channels through the cell membrane. Before depolarization, the Ca^{2+} concentration in the cytoplasm is about 6×10^{14} ions/cc. The Ca^{2+} concentration outside the neuron is about 10,000 times higher. Hence the depolarization enables calcium ions to flood into the neuron and trigger a cell response. Even a rather small change in intracellular calcium can exert profound changes in cellular activity, Bretscher (1985). In the synaptic terminals of neurons, for example, calcium induces the release of neurotransmitter molecules.

The extracellular fluid cannot be the sole source of calcium ions. For one thing the absence of extracellular calcium does not prevent external messenger acetylcholine from stimulating the pancreas to release the digestive enzyme amylase. Thus it has become apparent that calcium employed by a cell for internal signaling not only enters the cell from outside but is also released from internal reservoirs. There turn out to be many examples of hormones or neurotransmitters employing internal calcium to control physiological processes, Bretscher (1985).

Hence external stimuli which can cause influx or efflux of calcium ions from the cell have clear and important consequences for cell growth regulation, cell death, neurotransmitter and hormone balance.

12.2 Calcium ions and Electromagnetic Interactions:

A perspective on the EM properties involved can be seen by noting that the characteristic membrane potential of most cells is about 0.1 V in a resting state. Since this exists across the very thin (40 Å) plasma membrane, it creates an enormous barrier of the order of 10^5 V/cm. However imposed ELF and amplitude modulated RF fields produce tissue gradients in the range 10^{-7} to 10^{-1} V/cm, which are gradients involved in essential physiological functions in marine vertebrates, birds and mammals, Adey (1981). In vitro studies have reported similar sensitivities for cerebral Ca^{2+} efflux, and in a wide range of calcium-dependent processes that involve cell membrane functions, including bone growth, modulation of intercellular communication mechanisms that regulate cell growth, reduction of cell-mediated cytolytic immune responses, and modulation of intracellular enzymes in signal transduction. These processes have been confirmed for many human cell types, including lymphocytes, ovary cells, bone cells, fibroblasts, cartilage cells and nerve cells, Adey (1992a).

Since the electric field strength varies as the square root of the exposure (Eq. 3), for a 147 MHz modulated RF field with an environmental exposure of $1\mu W/cm^2$ or $0.1\mu W/cm^2$ the Tissue Gradients are estimated at 3.5×10^{-3} V/cm and 1.1×10^{-3} V/cm , respectively. These are still at least 10,000 times higher than the lower limit of 10^{-7} V/cm.

Calcium ion efflux from within cells clearly alters the intracellular calcium ion concentration, which alters the Calcium ion signal transduction process which is vital to balanced regulation of cell growth and, in neuron tissue, neurotransmitter and

neurohormone production and reception. In other tissue it alters the reaction to the stimulation of antibodies because the role of calcium ion homeostasis in activation of channels of cells in the immune system.

Luben (1995) summarizes research through which RF radiation which is modulated at ELF frequencies changes the calcium ion efflux in Table 5.

It is now widely accepted that calcium plays a central role in the development of the immune response, Grinstein and Klip (1989). Changes in the cytoplasmic free calcium concentration (Ca^{2+}) are thought to be essential for responses as varied as bacterial killing by neutrophils and the synthesis and secretion of antibodies by lymphoid cells.

It is pertinent to note that the "no effects" studies of Merritt et al. (1982) are consistent with the power intensity windows identified by Blackman et al. (1980a, 1988). It is well established that calcium ion efflux changes are not linearly related to intensity, but rather to particular combinations of intensity, modulation frequency and temperature range. It is also pertinent to note that although a great deal of calcium ion efflux research has focused on ELF exposures, the table 5 below is for modulated RF/MW exposure, with effects being found for carriers in the range 50 MHz to 915 MHz and modulation frequencies in the range 0.5 to 32 Hz.

Calcium ion signaling is a function of the central nervous system (CNS). Walleczek (1992) proposes that research findings show that membrane-mediated calcium ion signaling processes are involved in the mediation of ELF effects on the immune system. ELF modulated microwaves have similar effects.

Shandala et al. (1979) found that calcium ion efflux varies in living animal cells at $10\mu W/cm^2$ using microwaves (about 0.0075 W/kg), consistent with Kolomytkin et al. (1994).

The understanding of the role of intercellular calcium ions has been growing and evolving rapidly over recent years. The fact that ELF radiation, and RF/MW radiation which is modulated at ELF frequencies, significantly alters the calcium ion concentrations and efflux in intracellular fluid is well proven and documented down to SARs of 0.00015 W/kg. Electromagnetic fields, through their effect on calcium ions, play a vital role in the immune system, Walleczek (1992). Walleczek (1992) quotes research relating to the role of calcium, sodium and potassium ions, including research showing that EMF could alter the activity of the membrane incorporated Ca^{2+}-ATPase responsible for pumping Ca^{2+} out of the cell (calcium ion efflux).

In addition, data from two laboratories demonstrate that ELF fields alter the activity of another membrane ion pump, Na^+/K^+-ATPase with current densities as low as $50\mu A/cm^2$ and estimated, by the authors, to also have an effect at $1\mu A/cm^2$. At $50\mu A/cm^2$, J = 0.5

Table 5: Summary of Studies concerning Biological effects of Low Frequency Modulation of RF Radiation.

Effects	Species	RF (MHz)	Mod^n (Hz)	Intensity (mW/cm^2)	Time (min)	SAR (W/kg)	Reference
Altered calcium-ion efflux in brain tissue in vitro:							
Frequency specificity	Chicken	147	6-20	1-2	20	0.002*	Bawin et al.(1975)

influence of pH and lanthanum	Chicken	450	16	0.75	20	0.0035	Bawin et al.(1978)
frequency and intensity specificity	Chicken	147	16	0.83	20	0.0014	Blackman et al.(1979)
intensity specificity and sample spacing	Chicken	147	9,16	0.083	20	0.0014	Blackman et al.(1980a)
intensity specificity and sample spacing	Chicken	147	16	0.083	20	0.0014	Joines et al (1981)
intensity specificity	Chicken	450	16	0.1-1	20	0.005-0.005	Sheppard et al.(1979)
two intensity ranges	Chicken	50	16	1.5 3.6	20 20	0.0013 0.0035	Blackman et al.(1980b)
theoretical analysis of RF dependence	Chicken	50 147 450	16	-	20	~0.001	Joines and Blackman(1980) Athey (1981); Joines and Blackman (1981).
test of predictions of theoretical analyses	Chicken	147	16	0.37 0.49	20	0.0006 0.0008	Blackman et al.(1981)
no effect for pulse modulation	Rat	1000	16,32	0.5-15	20	0.15-4.35	Shelton and Merritt (1981)
no effect for pulse modulation	Rat	1000 2450	16 8,16,32	1,10 1	20	0.29-2.9 0.3	Merritt et al. (1982)
change in calcium efflux kinetics in synaptosomes	Rat	450	16	0.5	10	-	Lin-Liu and Adey (1982)
frequency and intensity specificity in cultured neuroblastoma cells	Human being	915	16	-	30	0.05	Dutta et al.(1984)
Altered calcium ion efflux in brain tissue in vivo:							
no effect for pulse mod.	Rat	2060	8,16,32	0.5-10	20	0.12-2.4	Merritt et al.(1982)
change in efflux kinetics	Cat	450	16	3	60	0.29	Adey et al.(1982)
Changes found in pancreatic slices	Rat	147	16	2	60-150	<0.075	Albert et al.(1980)
Suppressed T-lymphocyte	Mouse	450	16-100	1.5	120	-	Lyle et al.(1983)
Changes in Hearts	Frog	240	0.5,16		30	0.00015-	Schwartz et al (1990)

A/m^2; E=2.5 V/m, assuming σ=0.2 S/m. Hence from Eq.(1) S= 1.7 $\mu W/cm^2$ and SAR = 0.00063 W/kg from Eq.6 . If the extrapolation to 1$\mu A/cm^2$ is confirmed then the EMR effects will be occurring at $1/2500^{th}$ of the S and SAR levels estimated here.

This demonstrates the extremely low induced currents, SARs and energy densities which are associated with EMR induced changes in ion pumping and calcium, sodium and potassium efflux at the cellular level.

Walleczek and Budinger (1992) report that:

> **"To date, at least 10 different laboratories, including our own, have reported ELF magnetic influences on lymphoid cells, and stimulatory as well as inhibitory effects on parameters related to calcium metabolism or RNA- and DNA-synthesis have been observed."**

They also state that:

> **"A plausible magnetic interaction mechanism based on radical pair recombination reactions which are linked to cellular signal transduction and application processes has been proposed (Grundler et al. (1992)). Magnetic field intensities similar to the intensities used in most experiments (e.g. 1-30 mT) are known from magnetochemistry to be able to influence *non-thermally* the kinetics and product yields from radical pair reactions *in vitro*, Steiner et al. (1989). The underlying reaction scheme is well known and is described by the radical pair mechanism.**
>
> **For this mechanism to be applicable to the data reported here, a pathway by which magnetically-sensitive radical-dependent processes could influence mitogen-induced lymphocyte Ca^{2+} signaling must be postulated. There is new evidence that such pathways exist.**
>
> **For example, Con A-induced Ca^{2+} uptake in rat thymic lymphocytes has been shown to depend on the generation of reactive oxygen radical species. There is also evidence from inhibition studies that cytochrome P-450 activity may be involved in Ca^{2+} uptake regulation in rat thymic lymphocytes, Alvarez et al. (1992), and it is known that P-450 function proceeds via radical pair recombination steps, Hollenberg (1992). Thus it is plausible to investigate if externally applied magnetic fields may interfere with radical pair reactions and as a consequence, may alter lymphocyte Ca^{2+} regulation."**

Calcium ion influx has been shown to play a role in the transcript levels of proto-oncogenes c-myc and c-fos which alters in the presence of electromagnetic fields, Karabakhtsian et al (1994). (Proto-oncogenes: altered genes which become carcinogenic.)

Lindstrom et al. (1995) replicate and extend the research of Walleczek (1992), using the T-cell line (lymphocytes) for human leukaemia cells, and show that oscillating low-level magnetic fields produce the same calcium ion reaction as does an antibody. They show that weak magnetic fields initiate calcium ion oscillations with a threshold flux density of 40 μT, a plateau at 150 μT and a frequency range from 5 to 100 Hz, with a fairly broad peak at 50 Hz.

Galvanovskis et al. (1996) report significant 30% reductions in the calcium ion oscillation amplitude in human leukaemia T-cells when exposed to 50 Hz magnetic fields.

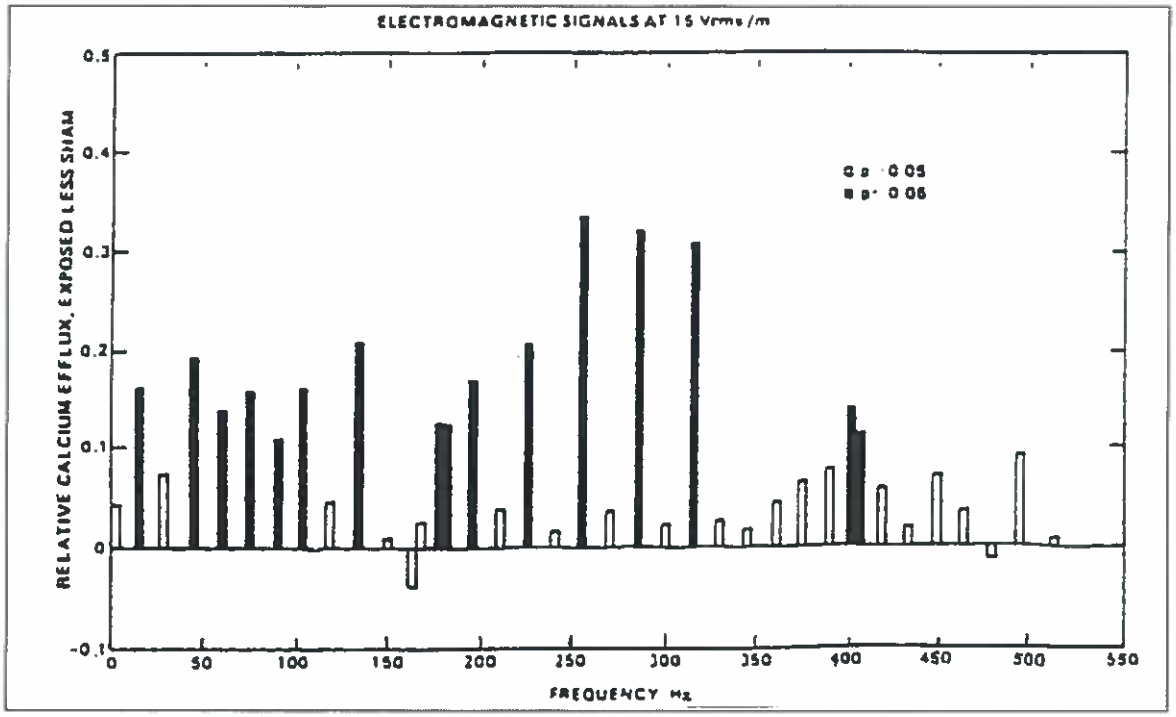

Figure 18: The effect of 15 V/m electromagnetic fields on the efflux of calcium ions from chicken brain tissue as a function of modulation frequency. The relative efflux is the difference between exposed and unexposed samples. The data from 1 to 120 Hz are taken from Blackman et al. (1985). Blackman et al. (1988).

The key role of modulation frequency in the alteration of calcium ions was recognized early. A leading researcher in this area, Dr Carl Blackman of the U.S.E.P.A. has shown that research has identified modulation frequencies which significantly alter calcium ion efflux out to 510 Hz, Figure 18.

This takes us away from the long term concentration on the 16 Hz calcium ion oscillation which first attracted attention. We can only speculate on what the results would have been in the above quoted experiments if the modulation of ELF frequency had been extended out to 500 Hz.

Their research further shows the involvement of polypeptide molecules, specifically poly-L-lysine, which the authors postulate may explain the intracellular calcium ion EMR effects on cell membrane surfaces, through the polylysine causing strong deformations on the cell surface which could trigger the release of stored calcium cations from intracellular pools, thus starting the oscillations. The authors conclude:

> **"These results allow us to suggest that 50 Hz; 100 μT magnetic fields might influence some step in the chain of biochemical events leading to the sustained calcium ion oscillation."**

They further note:

"That more than 20 enzymes are thought to incorporate radical chemistry in the conversion of substrates to products. It is possible that some enzymes or intermediates containing radicals are involved in the complex system responsible for intracellular calcium ion regulation. It has been shown that such biochemical reactions may be sensitive to the magnetic field."

12.3 Intensity and Frequency Windows:

Calcium ion efflux is shown to be enhanced in intensity and modulation frequency windows, suggesting a pseudo-quantum effect. The early work of Dr Susan Bawin and Professor Ross Adey, Bawin and Adey (1976) and Adey (1980) for example, identified differences with exposure intensity and modulation frequency suggesting intensity and frequency "windows" in relation to calcium ion efflux from chick brains. Much of this work was replicated by Dr Carl Blackman at the U.S.E.P.A., e.g. Blackman et al. (1989). In Blackman's paper he comments that they could not replicate the Bawin and Adey results until his team had carefully examined the power-density dependence of the field and discovering that only certain power densities and certain modulation frequencies were capable of eliciting the response. Blackman et al. (1989) found that at 16 Hz modulation of a 50 MHz carrier with a highest SAR of 0.005 W/kg was far to low to cause heating. They report that statistically significant effects were found at power densities of 1.44-1.67, 1.75, 3.85, 5.57, 6.82, 7.65, 7.77, and 8.82 mW/cm^2, but not at 0.37, 0.72, 0.75, 2.17, 2.30, 4.32, 4.50, 5.85, 7.08, 8.19, 8.66, 10.6, and 14.7 mW/cm^2 .

Blackman et al. (1989) propose a fractal process with a non-integer dimension of 1.4 to explain a series of highly peaked responses which correspond to cell membrane level amplicational processes. Using the probability of the statistical significance (p) which is $p<0.001$ for the strong peaks, they note that there is no decrease at the lower power densities making it impossible to extrapolate to a lowest threshold. Dr Adey has shown nonlinear dynamical responses at the cellular level for some time, but Dr Blackman and his group claim to be the first to apply fractal geometry to the problem and in doing so, open the possibility for functional alterations to the CNS due to very weak stimuli.

The lowest reported SARs with statistically significant increases in calcium ion efflux at 0.00015 and 0.0003 W/kg from Schwartz et al. (1990), using 16 Hz modulation and a 240 MHz carrier.

Blackman et al. (1991) define a temperature window for the calcium ion efflux from avian brain tissue. Effects are seen for 36 and 37°C but not for 35 and 38°C. The effects are evident within the normal core temperature range but not outside it.

These results, for power density and temperature windows, explain why no effects were seen in early experiments which used high power densities and raised the temperature of the sample. It is not a simple matter of higher exposure gives greater effects, i.e. there is not a simple dose-response relationship. The effects are highly quantized by particular sets of conditions which trigger cell membrane reactions which involve enzyme amplifiers in the signal transduction process which are thought to be poised at a phase or cooperative transition.

12.4 Calcium-ion Signaling Summary:

ELF and RF/MW modulated at ELF frequencies, change the oscillation frequency and amplitude and they change the influx and efflux of calcium ions in and around the cell membrane.

The changing oscillation frequency and amplitude is related to the immune response of the cell and shows that the oscillating applied field produces an antibody-like reaction as though the cell has been attacked.

The influx and efflux changes relate to the signal transduction pathway in which calcium ions participate. This is one of the biochemical pathways which regulate cell behaviour. This is altered by the applied oscillating electromagnetic field. Since signal transduction controls the cell division, cell differentiation and cell proliferation, this EMR induced alteration to signal transduction has the strong potential to participate in tumour formation or promotion. Alteration of T-lymphocytes and other immune system factors suggests that EMR exposure causes immuno-suppression, partly through induced calcium ion efflux.

The following section on DNA damage and chromosome aberrations is consistent with this. While research shows that DNA is damaged and chromosome aberrations are found in EMR exposed cells, animals and people, the evidence does not point to direct DNA breakage but to the involvement of free radicals or some other cellular level mechanism such as altered signal transduction pathways.

12.5 Calcium ion Conclusion:

Courtesy of Professor Ross Adey, Adey (1993):

> **"Life on earth has evolved in a sea of natural electromagnetic (EM) fields. Over the past century, this natural environment has sharply changed with the introduction of a vast and growing spectrum of man-made EM fields. From models based on equilibrium thermodynamics and thermal effects, these fields were initially considered too weak to interact with biomolecular systems, thus incapable of influencing physiological functions. Laboratory studies have tested a spectrum of EM fields for bioeffects at cell and molecular levels, focusing on exposures at athermal levels. A clear emergent conclusion is that many observed interactions are not based on tissue heating. Modulation of cell surface chemical events by weak EM fields indicates a major amplification of initial weak triggers associated with the binding of hormones, antibodies, and neurotransmitters to their specific binding sites. Calcium ions play a key role in this amplification. These studies support new concepts of communication between cells across barriers of cell membranes; and point with increasing certainty to an essential physical organization in living matter, at a far finer level than the structural and functional image defined by the chemistry of molecules. New collaborations between physical and biological scientists define common goals, seeking solutions to the physical nature of matter through a strong focus on biological matter. The evidence indicates mediation by highly nonlinear, nonequilibrium processes at critical steps in signal coupling across cell membranes. There is increasing evidence that these events relate to quantum states and resonant responses in biomolecular**

systems, and not to equilibrium thermodynamics associated with thermal energy exchanges and tissue heating."

13. Free Radicals

13.1 Introduction:

A free radical is an extremely reactive molecule which carries an unpaired electron and which has a very short half-life of 10^{-5} s or less. Although superoxide anions (O_2^-) are the primary oxygen radicals produced in biological systems, they can also give rise to a cascade of other radicals such as hydroxyl, carbonate and lipoperoxy radicals.

Medical literature documents the role of free radicals in carcinogenesis, Guyton and Kensler (1993):

"Cancer in humans and animals is a multistep disease process. In this process, a single cell can develop from an otherwise normal tissue into a malignancy that can eventually destroy the organism. The complex series of cellular and molecular changes that occur through the development of cancers can be mediated by a diversity of endogenous and environmental stimuli. Active oxygen species and other free radicals have been known to be mutagenic; further these agents have more recently emerged as mediators of other phenotypic and genotypic changes that lead from mutation to neoplasia. Free radical production is ubiquitous in all respiring organisms, and is enhanced in many disease states. Free radicals may therefore contribute widely to cancer development in humans."

13.2 Cumulative effects:

Commonly used chemicals and drugs produce damaging levels of free radicals, which produce chromosome and DNA damage and suppress the immune system. Enwonwu and Meeks (1995) review the free radical chemistry of tobacco and alcohol in relation to oral cancer. The abstract is included here to illustrate the central role of free radicals in cancer and immune system suppression, whether they are produced by chemicals, ionizing radiation or non-ionizing electromagnetic radiation. They also address the role of free radical scavengers, such as anti-oxidants.

"Abstract :

As shown in this report, abuse of alcohol and tobacco has serious nutritional implications for the host, and generates increased production of reactive free radicals as well as eliciting immunosuppression. Maintenance of optimal competence of the immune system is critical for cancer surveillance. Active oxygen species and other reactive free radicals mediate phenotypic and genotypic alterations that lead from mutation to neoplasia. Consequently, the most widely used chemopreventive agents against oral cancer (e.g., vitamins A, E, C, and beta-carotene) are anti-oxidants/free radical scavengers. These anti-oxidants, both natural and synthetic, neutralize metabolic products (including reactive oxygen species), interfere with activation of procarcinogens, prevent binding of carcinogens to DNA, inhibit chromosome aberrations, restrain replication of the transformed cell,

suppress actions of cancer promoters, and may even induce regression of pre-cancerous oral lesions such as leukoplakia and erythroplakia.

13.3 EMR effects on free radicals:

Modulated EMR has been shown to reduce melatonin levels and to lead to an increase in free radicals and increased cell death.

Barnett (1994) reviews possible mechanisms relating microwave exposure to the action of free radicals:

> **"There is increasing support for the theory that free radicals play an important role in discrete, important sub-cellular events during exposure to microwaves. The field of magneto-chemistry is beginning to have an impact on the understanding of subtle effects in molecular biology of cell systems. Chemical bonds consist of paired electrons with opposite spins. Free radicals are highly charges and can only form bonds between radicals of opposite spins. Electron spins may be altered by EM fields and radicals prevented from uniting. Recent information on the small unstable molecule, nitric oxide (NO), as a physiological mediator has shown the importance of oxygen free radicals in biological systems. NO is understood to modulate neurotransmission and regulate cerebral arterial blood flow and has been implicated in the pathogenicity of Alzheimer's Disease.**
>
> **Microwave-induced lowering of phase transition temperature and increasing membrane permeability is inhibited by the presence of antioxidants, thereby implicating free radical involvement. A number of laboratories have reported enhanced permeability to sodium cation in erythrocytes during exposure to microwave fields."**

Adey (1993) discusses McLauchlan (1992) which proposes a model for the production of free radicals by ELF fields. McLauchlan concludes from his model that "the effect begins at the lowest applied field strength, even at levels below thermal noise (kT). The all-important interaction has an energy very much less than the thermal energy and is effective exclusively through its influence on the dynamics; this is counter intuitive to most scientists." Adey (1993) goes on to consider the work of Grundler and Keilmann (1978) and Grundler and Kaiser (1992) in which around 42 GHz they found highly tunes resonances in yeast cells, with clear responses down to 5 picowatt/cm^2.

Grundler et al. (1992) present a synthesis of interaction of nonthermal EM fields with cellular systems. They present a model of EM field transductive coupling, based on magnetic field-dependent chemical reactions, including cytochrome-catalyzed reactions that involve free radicals, such as reactive oxygen or nitric oxide, leading to a further highly cooperative amplification step. They conclude that in such a system "imposed fields can be active even at intensities near zero."

Lai and Singh, pers. comm. have exposed rat brains to sub-thermal pulsed microwaves (2.45 GHz) and found enhanced single- and double-strand DNA breakage in the presence of enhanced free radicals and accelerated cell death.

The models are now being confirmed by experiments in living tissue as laboratory techniques allow detection of cellular level effects. It is highly likely that the many examples of observed chromosome damage in the presence of RF/MW fields is due to the involvement of free radical mechanisms and/or disruption to intra- and inter-cellular communication. The consequence of this is impairment of the immune system and increased risk of cancer and birth defects, for example.

14. Carcinogenesis processes:

14.1 Introduction:

It has been estimated that 75-80% of all human cancers are environmentally induced, Clemens (1991), 30-40 % of them by diet. The remaining cancers, 35-50%, are primarily from environmental toxins, among which epidemiological research strongly implicates electromagnetic radiation.

Two distinct types of process which lead to neoplasm of cells which can lead to malignant cancer can involve electromagnetic radiation, signal transduction alteration and genetic damage. The first involves the change in signal transduction process in the cells which controls the cells development, and involves calcium ions and/or ODC for example, Byus (1994), Luben (1995), and Weinstein (1991). The second involves DNA and chromosome damage through the action of such agents as free radicals.

A multi-stage process for developing cancer is often described. This starts with initiation, then promotion and finally progression, Weinstein (1988). Adey (1992b) adds "synergism" to include the effects of co-carcinogens, Figure 21.

Initiation involves a single exposure to a carcinogen which damages the nuclear DNA. A single agent (a complete carcinogen) or two or more agents may be necessary, working together in the proper sequence. Promotion involves multiple exposures at certain intervals to agents which do not damage DNA directly. Promotion leads to conversion from benign to malignant tumours. Progression involves the increasing degree of malignancy.

The latency period for most cancers (the time between initiation and appearance of the disease) is often 20 years or more. Initiation is generally thought to change the cell's genetic stores of DNA, but the change is not expressed and a tumour does not result unless one or more promoting agents act repeatedly at a later time. Initiated cells may remain quiescent if they are not stimulated by a promoter, and cancer may never develop if sufficient exposures to promoters do not occur.

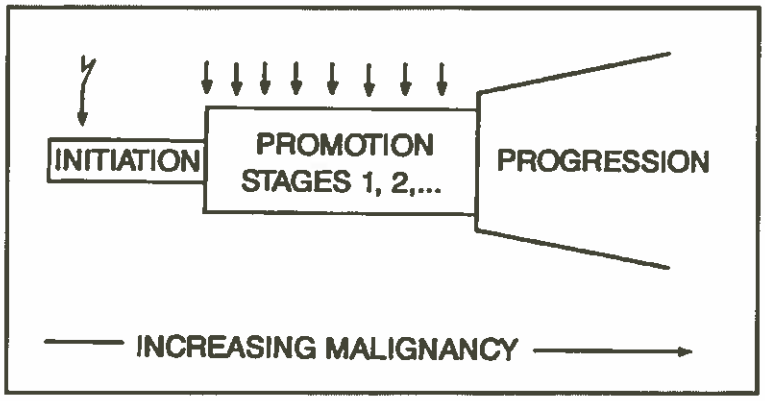

Figure 21: Model of multistage carcinogenesis from studies in mouse skin. Initiation results from only a single exposure to a carcinogen that appears to damage nuclear DNA. Promotion involves multiple exposures at certain intervals to agents that do not damage DNA directly. Promotion leads to conversion of benign to malignant tumours, with progression increasing the degree of malignancy. (After Weinstein, 1988).

In a specific context, tobacco proteins are both initiators and promoters. Because of cigarette smoking's promotional attributes, risks of lung cancer decline after a smoker rejects the habit.

Promotion and progression agents have very weak or no carcinogenic activity when tested alone, but they markedly enhance tumour yield when applied repeatedly following a low or sub-optimal dose of a carcinogen. Promoting agents are not mutagenic and thus are not cancer initiators by an action on the DNA in the nucleus.

Many papers give evidence of EMR as a cancer promoter, e.g. Adey (1992b). Agents which disrupt the gap-junction communication or alter the signal transduction in order to increase proliferation, can be cancer promoters. EMR does change these cellular processes in the same way that known cancer promoters do. In cell cultures the ability of T-lymphocytes (T-cells) to destroy tumour cells is shown, pointing to the importance of the immune system in reducing and eliminating cancer cells. Both 60 Hz ELF and modulated RF fields (450 MHz) fields, Lyle et al. (1983), reduce the lymphocyte killing ability.

Synergism is another form of interaction which occurs when two or more substances potentiate each other's actions, producing more cancers than can be accounted for by the separate effects of each. The phorbol ester TPA is known to activate the membrane bound enzyme protein kinase C (PKC). Studies of these interactions show that PKC plays a critical role in signal transduction in normal cells and it is irreversibly activated by phorbol esters, Adey (1992b). PKC belongs to a group of cAMP-dependent protein kinases identified as sensitive to weak RF fields amplitude-modulated at ELF frequencies, Byus et al. (1984). Many experiments in cell-lines and in animals have shown synergistic effects of EMR and chemical cancer promoters, benzpyrene or TPA for example.

However, evidence is growing that ELF modulated RF/MW radiation not only alters the cellular level growth regulation processes in a cancer promoting way, but also is involved under some circumstances in the breakage of nuclear DNA. Hence EMR appears to be both a cancer initiator and a cancer promoter, which also enhances progression. In this

way the similarity with cigarettes is quite strong, as are the similarities to the effects of ionizing radiation, but at a lower, but not insignificant level of impact, particularly because of the near universal exposure of people to RF/MW radiation.

14.2 DNA breakage and Chromosome aberrations (CA) by EMR:

Carcinogenesis can be initiated through breakage of DNA which leads to the aberration of chromosomes. This can happen by the direct action of free radicals or by the inactivation of tumour suppresser genes. Thus it is generally accepted that chromosomal mutations are causal event in the development of neoplasia, Hagmar et al. (1994). Hence, at the population level, an increased frequency of CA has thus been generally considered indicative of increased cancer risk for those exposed to the damage-inducing agent. Thus it is important to review research which shows CA under EMR exposure.

Two of the important agents identified in these processes are melatonin and free radicals, Liburdy et al. (1993), Reiter (1994) and possibly also calcium ions. CA may be enhanced directly by physiological responses to EMR which reduce the production of melatonin or indirectly by substances such as cysteamine which enhance free radicals. This effect was found in by Kondo et al. (1985) when investigating DNA damage observed after exposure to 1.2 MHz infrasound. Alternatively they may impair the DNA repair mechanism, by altering the cell cycle for example. In either case the result is damaged nuclear DNA.

14.3 Early Biomedical Result: Pulsed RF breaks chromosomes.

Nature, in March 28th, 1959 contains a paper in the Genetics section entitled "A New Physical Method of creating Chromosome Aberrations". The authors, Drs Heller and Teixeira-Pinto at the New England Institute for Medical Research, report a method they use to prepare medical samples which contain high levels of chromosome aberrations. They use a radiofrequency source of 27 MHz, a pulse length of about 50μs and between 80 and 180 pulses per second (pps).

They report asymmetrical particles aligning themselves along the field lines. They observe that motile bacteria or protozoa migrate along field lines when the RF is on, but resume random movement when the field is turned off. This can be repeated as often as desired. They note that the thermal component is so low as not to affect the viability of these organisms or of mammalian cells. No increase of themperature of the water was noted. In the larger organisms, they were able to observe intracellular orientation of the subcellular particles. They say that this led them to believe that this force might be used as a powerful and controlled mutagenic agent.

Growing garlic roots were exposed to the field and the water they were in was monitored and no temperature rise was seen. The tips were exposed to the RF field for 5 mins and examined 24 h later. They observe, Heller and Teixeira-Pinto (1959):

> **"Among those aberrations seen were linear shortening of chromosomes, pseudochiasmata, amitotic division, bridging, irregularities in the chromosomal envelope. The effects noted mimic those produced by ionizing radiation and c-mitotic substances."**

Of the papers and reviews I have, it is only cited in Shore (1981), the WHO review "Environmental Health Criteria 16: Radiofrequency and Microwaves" This short paper is

remarkable for its significance and the fact that it is been almost totally ignored by subsequent reviews and reports. The conclusion about the similarity of effects to those of ionizing radiation and other cell damaging agents is telling. It also related to the role of free radicals, which are known to be produced and cause DNA damage under exposure to ionizing radiation and have been observed in vivo under microwave exposure, Lai and Singh pers. comm. It is also noted in a mouse reproductive study by Dimberg (1995), who used 20 kHz magnetic field with a peak-to-peak amplitude of 15 μT (sawtooth wave). He concludes: "Most of the effects of MF (magnetic field) treatment during the embryonic period were similar to those induced by ionizing radiation but much weaker".

14.4 ELF studies involving chromosome aberrations, DNA breakage and cancer:

Several ELF exposure studies have been carried out on workers which are of relevance because to the strong similarity between effects of ELF EMR and ELF modulated RF/MW EMR. As noted above the effect of RF/MW modulated by ELF should be even stronger than ELF alone because of RF/MW penetrative effects into mammal bodies.

Murphy et al. (1993) note that since epidemiologic studies have reported a modestly increased risk of childhood leukemia associated with certain electric power wire configurations and since cancer it likely to involve DNA damage, this review discusses the evidence of direct and indirect genetic toxicity effects for both electric and magnetic fields at 50- and 60-Hz and miscellaneous pulsed exposures. Exposure conditions vary greatly among different end points measured, making comparisons and conclusions among experiments difficult. Also in 1993 Liburdy et al. (1993) provided "The first evidence that ELF frequency magnetic fields can act at the cellular level to enhance breast cancer cell prolifieration by blocking melatonin's natural oncostatic action. In addition there appears to be a dose threshold between 2 and 12 mG."

Lai and Singh (1997a) used a highly sensitive microgel electrophoresis, COMET assay technique to identify single strand DNA breaks, Figure 22, and double strand DNA breaks, Figure 23, from 2hr exposure to 0.1 mT and 0.25 mT 60 Hz magnetic fields in living rat brains.

Lai and Singh (1997a) conclude:

> **"Because DNA strand breaks may affect cellular functions, lead to carcinogenicity and cell death, and be related to the onset of degenerative diseases, our data may have important implications for possible health effects of exposure to 60 Hz magnetic fields."**

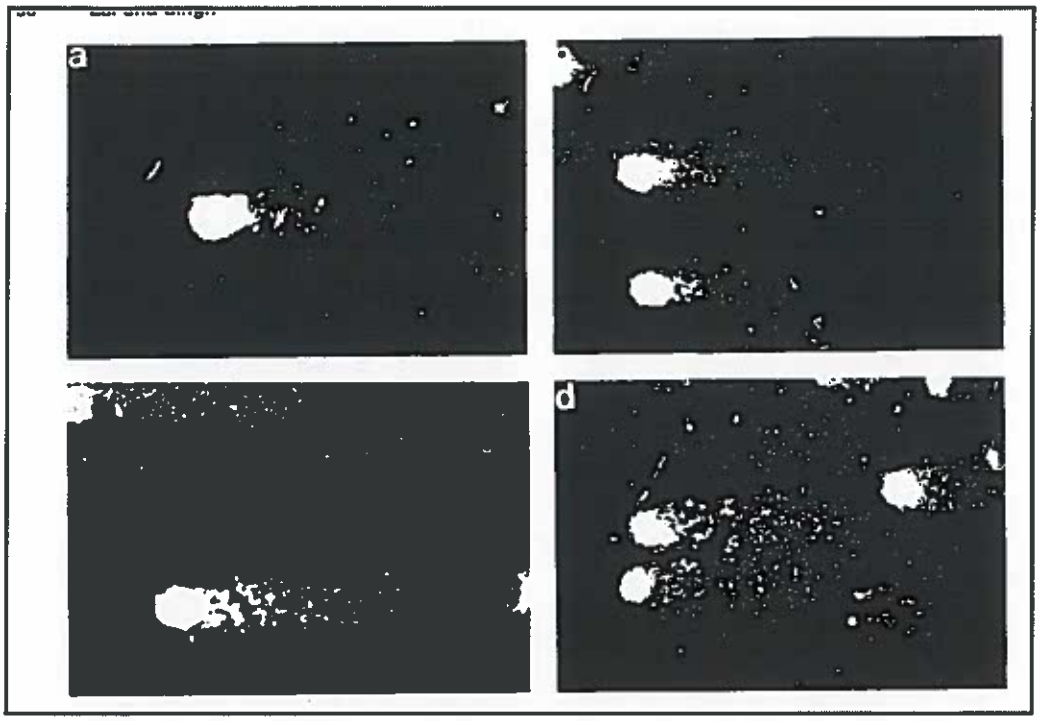

Figure 22: Photographs of single-strand DNA migration pattern of individual brain cells from rats exposed to (a) a bucking condition (0.1mT), magnetic fields of (b) 0.1 mT, (c) a 0.25 mT and (d) 0.5 mT. (x 400)

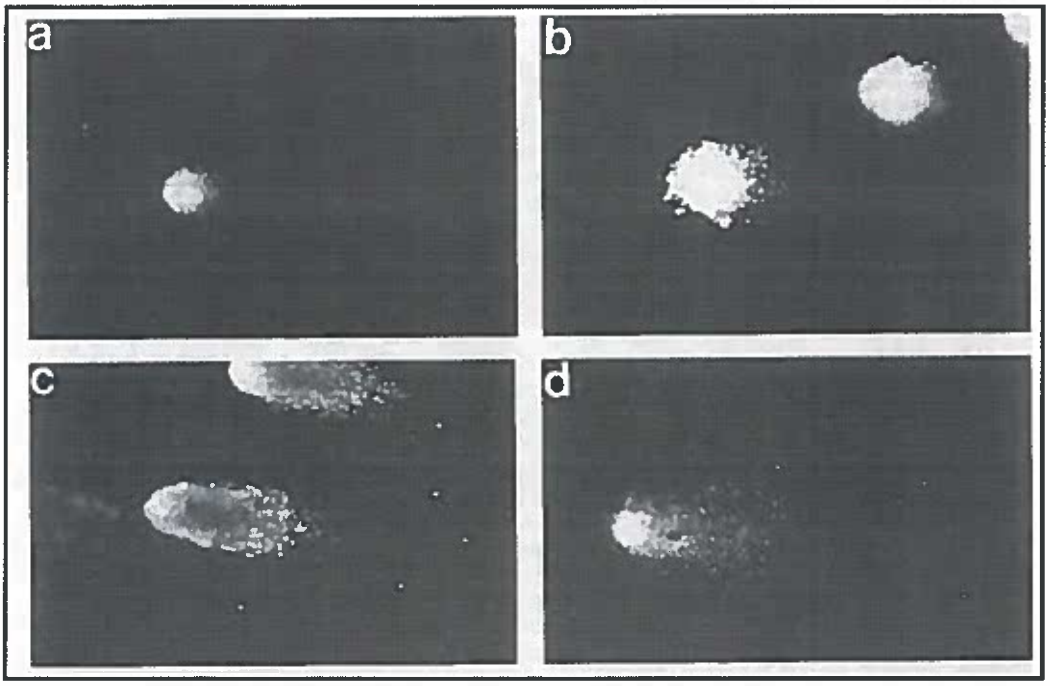

Figure 23: Photographs of double-strand DNA migration pattern of individual brain cells from rats exposed to (a) a bucking condition (0.1mT), magnetic fields of (b) 0.1 mT, (c) a 0.25 mT and (d) 0.5 mT. (x 400)

Lai and Singh (1997b) investigated the effect of melatonin and a spin trap compound (PBN) both of which scavenge free radicals. They found that rats injected with melatonin or PBN before ELF field exposure and 2 hours after exposure. Both of these treatments blocked the magnetic field induced DNA single- and double-strand breaks.

Lai and Singh (1997b) conclude:

> **"Since melatonin and PBN are efficient free radical scavengers, these data suggest that free radicals may play a role in magnetic field-induced DNA damage."**

Lai and Singh further state that both melatonin and PBN can have other actions on cells in the brain that can prevent DNA damage therefore further support for their hypothesis can be obtained by studying whether other free radical scavenging compounds also block the effect of magnetic fields.

Ciccone et al. (1993) conducted a case control study of 50 acute myeloid leukemias (AML), 17 chronic myeloid leukemias (CML), 19 myelodysplastic syndromes (MDS), and 246 controls. The chromosome aberrations were recorded according to the International System for Human Cytogenetic Nomenclature. Chromosome aberrations were not associated with chemical exposures (OR = 1.0), but a non-statistically significant excess was noted in association with electromagnetic fields (OR = 2.1).

Valjus et al. (1993) sampled for chromosomal aberrations, sister chromatid exchanges (SCEs), replication indices and micronuclei in peripheral blood lymphocytes among 27 nonsmoking power linesmen with considerable long-term exposure to 50-Hz EM fields, and among 27 nonsmoking telephone linesmen serving as a reference group, pairwise matched with the exposed workers for age and geographical region. Blood samples from the two groups were collected, cultured and analyzed in parallel. No differences between the groups were observed on analysis of SCEs, replication indices or micronuclei. However, the mean rate of lymphocytes with chromatid-type breaks was higher among the power linesmen (0.96% gaps excluded, 1.41% gaps included) than among the reference group (0.44% and 0.70%, respectively). The excess of aberrant cells was concentrated among those power linesmen who had worked earlier in their life. Although the interpretation is somewhat complicated by the confounding effect of previous smoking, these results suggest that exposure to 50-Hz EM fields is associated with a slight increase in chromatid breaks.

Skyberg et al. (1993) studied 13 high-voltage laboratory employees and 20 referents participated in a cross-sectional, matched-pairs study of cytogenetic damage. During cable testing the workers were exposed to static, alternating, or pulsed electric and magnetic fields. The alternating magnetic field levels of 50 Hz were 5-10 μT, occasionally much higher. Chromosome aberrations, sister chromatid exchanges, and aneuploidy were studied in peripheral blood lymphocytes. Among seven smoking laboratory employees the mean number of chromosome breaks/200 cells was 2.3, as compared with 0.7 for the job-matched referents. The comparable figures for inhibited cultures were 12.0 versus 6.0. No increase was detected in nonsmokers with either method. The results support, to some extent, the hypothesis of an increased risk of genotoxic effects among high-voltage laboratory workers, particularly a synergistic effect with smoking.

Nordenson et al. (1994) reported that their recent studies have shown a significant increase in the frequency of chromosomal aberrations in human amniotic cells after exposure to a sinusoidal 50 Hz, 30 μT (rms) magnetic field. To evaluate further interactions between chromosomes and electromagnetic fields, they analyzed the effects of intermittent exposure. Amniotic cells were exposed for 72 h to a 50 Hz, 30 μT (rms) magnetic field in a 15 s on and 15 s off fashion.

Eight experiments with cells from different fetuses were performed. The results show a 4% mean frequency of aberrations among exposed cells compared to 2% in sham-exposed cells. The difference is statistically significant, with $P < 0.05$ both excluding and including gaps. In another series of eight experiments, the cells were exposed in the same way but with the field on for 2 s and off for 20 s. Also in these experiments a similar increase in the frequency of chromosomal aberrations was seen, but only when the analysis included gaps. Continuous exposure for 72 h to 300 μT, 50 Hz, did not increase the frequency of chromosomal aberrations.

14.5 RF/MW studies:

Garson et al. (1991) studied 38 Australia Telecom radio-linesmen who had been exposed to RF EMR in their work and compared the chromosome damage in lymphocytes compared 38 non-exposed clerical staff. A very detailed assay of chromatid and chromosome gaps and breaks and other aberrations was carried out. Most categories showed a small but statistically insignificant increase in chromosome aberrations, with the sum of aberrations of 2.55% for linemen and 2.18% for controls (RR= 1.17, 95%CI: 0.9-1.6).

For Chromatid Gaps RR=1.2 (0.7-2.1); Chromosome Gaps: RR = 1.5 (0.6-3.5); and Chromosome Breaks (without outlier) 1.4 (0.8-2.3). Adjusting for confounding from recent X-rays and for smoking both produced a small increase in Rate Ratio. The absence of adjusting for coffee drinking is a limitation. Such an adjustment would be likely to favour reduction in the incidence among clerical workers, further increasing the Rate Ratio. The incidence of total chromosome aberrations among the controls does appear rather high.

Hagmar et al. (1994) trichotomize CA into the low (1-33%ile), medium (34-66%ile) and high (67-100%ile). The threshold for low CA is typically 1.0% but in the range 0.5 to 1.5 %, while medium is typically 1.0 to 2.0 %, and high >2 %, but may use a threshold between medium and high of 3 %. Taking the typical classification the Australia Telecom study gas both exposed and control groups in the high category. If the control group was in the "low" category <= 1%, then the Rate Ratio for the clerical staff would be 2.2 and for the linesmen 2.6, both of which are significant ($p<0.01$).

Timchenko and Ianchevskaia (1995) concluded that an electromagnetic field (EMF) at a frequency of 24 or 14 MHz and intensity of 400 or 200 V/m, increases numbers of epatocytes from rats with chromosomal aberrations 1.4-1.5-fold.

14.6 DNA breakage associated with RF/MW exposure:

Sagripanti and Swicord (1986) showed that non-thermal levels of microwave exposure can produce single and double-strand DNA breaks in E. coli in solution.

Garaj-Vrhovac et al. (1991) showed that cultured V79 Chinese Hamster fibroblast cell exposed to continuous wave (CW) 7.7 GHz microwaves at power density of 0.5 mW/cm^2 for 15, 30 and 60 min produced a significantly high frequency of specific chromosome aberrations such as dicentric and ring chromosomes in irradiated cells. The dose-response relationships were significant at $p<0.01$.

Garaj-Vrhovac et al. (1992) exposed whole human blood samples to the same exposure regime. With the addition of power densities of 10 and 30 mW/cm^2. The number of chromosome aberrations increased from 1.5 % in controls to 2.7 to 7.2 % at the rising power densities. There was a statistically significant dose response with $p<0.05$ for total aberrations, $p<0.001$ for Accentric and $p<0.0001$ for micronuclei.

Sarkar et al. (1994) found significant modification of the DNA from mouse cells from brain and testes exposed to 1 mW/cm^2 2.45 GHz microwaves for 2 hr/day for 120, 150 and 200 days.

Lai and Singh (1995) exposed living rats brains to a single 2 h exposure to microwaves at 2.45 GHz, pulsed at 500 pps, at SARs of 0, 0.6 and 1.2 W/kg. They found significant dose-response relationships for single strand DNA breaks in an assay carried out 4 hours after exposure for both the hippocampus and the rest of the brain. A second analysis involved assaying the whole brain and continuous wave microwaves at 2.45 GHz and 1.2 W/kg. This showed a statistically significant increase in single-strand DNA breaks between sham and exposed ($p<0.01$) but no significant difference between assays at 0 h and 4 h after exposure.

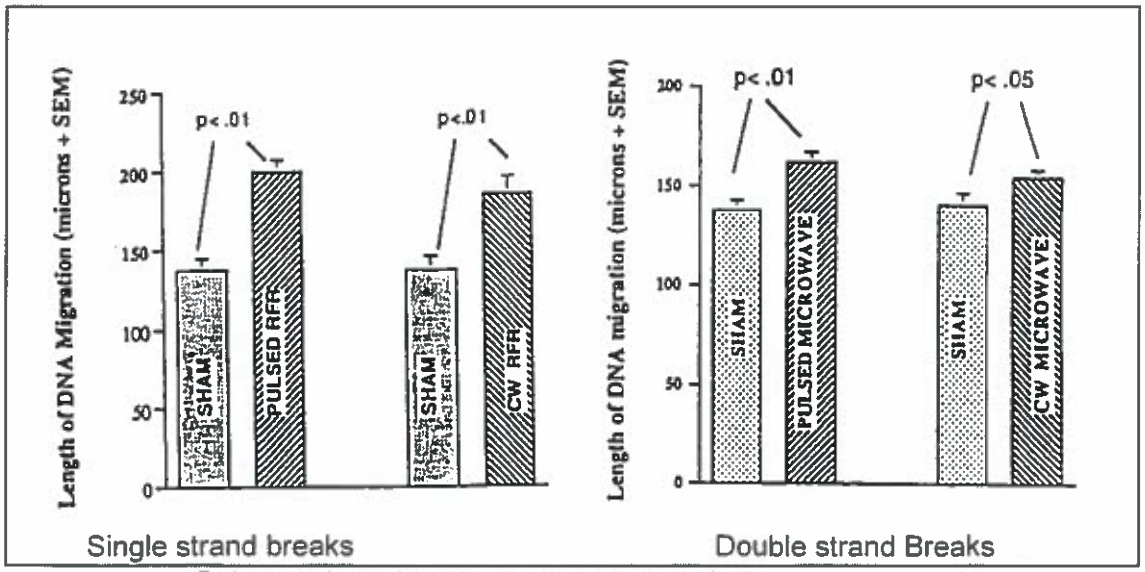

Figure 24: DNA breakage in rat brains (SAR = 1.2 W/kg), Lai and Singh (1996).

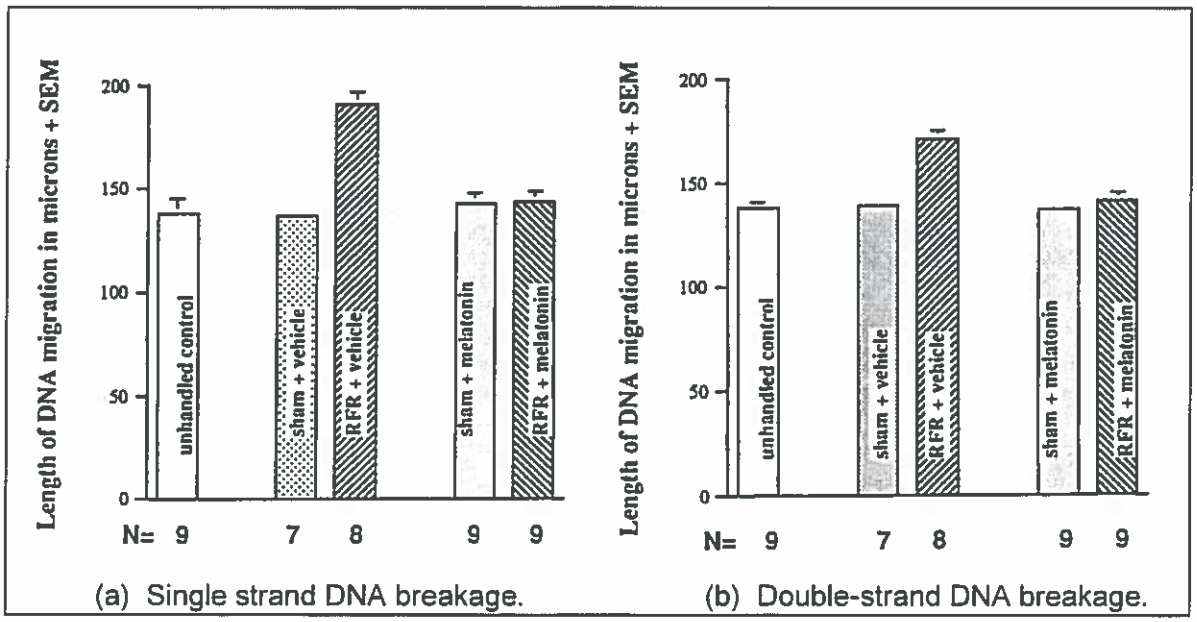

Figure 25a: Effect of melatonin on RF/MW induced DNA breakage, Lai and Singh (1997c).

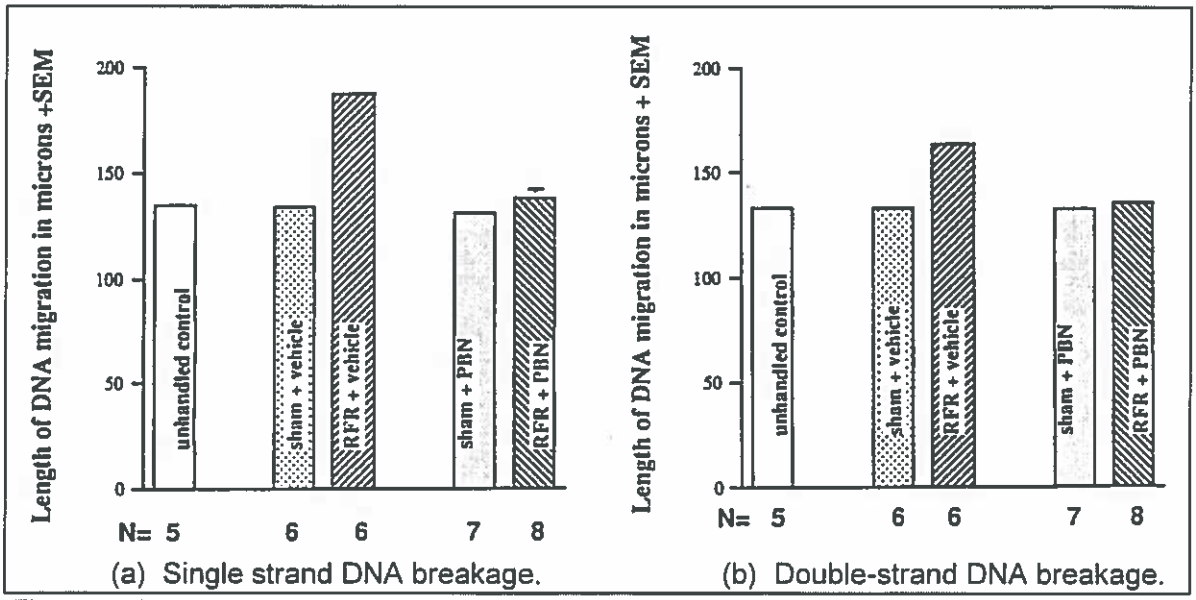

Figure 25b: Effect of PBN (spin-trap compound) on RF/MW induced DNA breakage, Lai and Singh (1997c).

Lai and Singh (1996) repeated the experiment of Lai and Singh (1995) and extended the analysis to include and assay of double-strand DNA breaks and included both pulsed (500 pps) and continuous microwaves at 2.45 GHz. The exposed condition was 2mW/cm^2 (SAR = 1.2 W/kg). Statistically significant single-strand DNA breaks were found for both the CW and pulsed signals ($p<0.01$), and for double-strand DNA breaks (pulsed $p<0.01$ and CW $p<0.05$). This data was not available for the MacIntyre Case.

Their most recent work, Lai and Singh (1997c), shows that in the exposed rats brains there is enhancement of free radicals and the acceleration of cell death (apoptosis), which

is eliminated by melatonin. It is not yet known whether this is caused by the MW radiation influencing the pineal gland or the retina of the eyes, to reduce melatonin production and hence enhance free radical numbers, or whether the MW radiation produces free radicals locally in the brain.

The implications of this study are very important. The authors, Lai and Singh (1997c), conclude:

"Data from the present experiment confirm our previous find in a [Lai and Singh, 1995, 1996] that acute RFR exposure causes an increase in DNA single- and double-strand breaks in brain cells of the rat. In addition, we have found that the effect can be blocked by treating the animals with melatonin or PBN. Since a common property of melatonin and spin-trap compounds is that they are efficient free radical scavengers [Carney and Floyd, 1991; Carney et al., 1991; Floyd, 1991; Lafon-Cazal et al., 1993 a,b; Lai et al., 1986; Oliver et al., 1990; Reiter et al., 1995; Sen et al., 1994; Zhao et al., 1994], these data suggest that free radicals may play a role in the RFR-induced DNA single- and double-strand breaks observed in brain cells of the rat. Consistent with this hypothesis is the fact that free radicals can cause damage to DNA and other macromolecules in cells. Particularly, oxygen free radicals have been shown to cause DNA strand breaks [McCord and Fridovich, 1978]. In addition, a study has implicated free radicals as the cause of some of the biological effects observed after exposure to RFR. Phelan et al. [1992] reported that RFR can interact with melanin containing cells and lead to changes in membrane fluidity consistent with a free radical effect.

If free radicals are involved in the RFR-induced DNA strand breaks in brain cells, results from the present study could have an important implication on the health effects of RFR exposure. Involvement of free radicals in human diseases, such as cancer and atherosclerosis, have been suggested. Free radicals also play an important role in aging processes [Reiter, 19951. Aging has been ascribed to accumulated oxidative damage to body tissues [Forster et al., 1996; Sohal and Weindruch, 19961, and involvement of free radicals in neurodegenerative diseases, such as Alzheimer's, Huntington's, and Parkinson's, has also been suggested [Borlongan et al., 1996; Owen et al., 1996]. Furthermore, the effect of free radicals can depend on the nutritional status of an individual, e.g., availability of dietary antioxidants [Aruoma, 1994], consumption of ethanol [Kurose et al., 1996], and dietary restriction [Wachsman, 1996]. Various life conditions, such as psychological stress [Haque et al., 19941 and strenuous physical exercise [Clarkson, 1995], have been shown to increase oxidative stress and enhance the effect of free radicals in the body. Thus, one can speculate that some individuals may be more susceptible to the effects of RFR exposure.

However, it must be pointed out that both melatonin and PBN can have other actions on cells in the brain that can decrease DNA damage. Further support for our hypothesis can be obtained by studying whether other compounds with free radical scavenging properties can similarly block the effect of RFR, and by measurement of other free radical-related cellular effects, such as oxidative molecular damages in lipids, protein, and DNA."

This is also relevant to the study carried out by Adey et al. (1996) in which rats exposed to cellphone-like signals had 30 % fewer tumours than controls and the tumours were statistically significantly smaller. These results were reported to the 1996 BEMS conference in Victoria BC. Dr Singh raised the question with Dr Adey, of the possibility of cell death as an explanation for the result. Dr Adey agreed that this was possible, but stated that it needed to be tested. Lai and Singh (1997c) have found that result.

It has been shown that a sub-thermal dose of microwaves (0.6 W/kg and 1.2 W/kg) can enhance DNA breakage and accelerate the cell death (apoptosis) in living brains, through the increased production of free radicals. This is associated with a reduction in melatonin. With enhanced rate of cell death tumour cells can die at a faster rate than they grow, producing fewer and smaller tumours.

All of these above experiments were carried out without the use of cancer initiators nor co-carcinogens. They involve the direct application of RF/MW radiation to a sample or an animal and the observation of chromosome breakage, DNA breakage, tumours, free radicals and cell death. Hence they confirm the proposal of Reiter (1994) in section 4.1, that EMR would be both an initiator and promoter of cancer, in his case through melatonin reduction, in this case through direct observation of DNA damage which might involve melatonin reduction since free radicals are observed to be enhanced.

14.7 Cellular Base Station radiation's synergistic mutagenic effect with MMC:

A Belgian research team has found that "very-close-range" exposure to microwaves from a cellular telephone base station increases the effect of a chemical mutagen on human blood cells, Maes et al. (1996). Whole blood samples were exposed to 954 MHz microwaves from an actual GSM base station and then to the DNA damaging agent mitomycin C (MMC). Other samples were exposed to either microwaves or MMC alone.

The exposure was at 5 cm from a GSM digital 15 W antenna, giving an SAR of 1.5 W/kg, for a period of 2 h and S = 514 $\mu W/cm^2$. This is a high, but significantly non-thermal exposure.

In this experiment, base station levels of microwaves alone showed no significant mutagenic effects. However, blood samples exposed to microwaves and then to MMC showed a considerably higher, statistically significant number of chromosomal abnormalities than those exposed to MMC alone. Microwave exposure increased the subsequent effect of MMC by about 20 to 50 %, the higher levels being produced by higher concentrations of MMC.

It is important to determine what the dose-response relationship of this exposure is. Clearly a non-thermal mechanism is operating, as will many other chromosome aberration observations reported here. These results show that GSM digital microwave radiation is co-carcinogenic with other natural or environmental carcinogens.

Thus people who are exposed to GSM bases station microwaves might have a higher risk of cancer and reproductive effects by making chemical carcinogens more potent in damaging chromosomes. A potentizing effect with skin cancer and UV is a possibility.

On the other hand, the research of Lai and Singh shows that the microwave exposure levels produced by cellular telephones in users heads, free radical production is enhanced, breaking DNA and enhancing the rate of cell death in the brain. The Belgian

research also suggests that the head's exposure to the cellular telephone antenna could enhance the risk of chemical damage of chromosomes.

14.8 Conclusions on Mutagenic effects of EMR:

Chromosome Aberrations and DNA damage has been found under non-thermal exposure to EMR. ELF and ELF modulated RF have been associated with chromosome aberration in cells and in exposed workers. Microwaves have been shown to produce DNA damage in living rats brains. Microwaves have also been shown to potentize cancer initiators (MMC) and to enhance the chromosome aberrations with exposure to a GSM digital base-station near field signal. Hence EMR is implicated in increasing cancer rates in exposed populations, Hagmar et al. (1994).

Increased cancer incidence can come about by the direct effect of a DNA damaging carcinogen or by the synergistic effect of co-carcinogens. The co-carcinogenistic effect and cancer promotional effect of EMR has been widely suggested and demonstrated through a number of experiments, e.g. Adey (1992b), Byus et al. (1988). Direct effects (in the absence of a cancer initiator) include chromosome aberrations and DNA breakage which is most likely to be the result of the enhanced presence of free radicals in the RF/MW field. The role of melatonin is important here. Direct effects are likely to involve higher mean power densities than co-carcinogenic effects. In Lai and Singh (1995) the inter-animal variability is very small giving a small standard deviation for each exposure group. Even so a linear the dose-response relationship is statistically significant for the "rest of the brain" assayed 4 h after exposure ceased. This suggests that the smallest detectable increase in DNA breakage would be associated, with this small sample size, with an SAR of <0.2 W/kg , σ = 1.7, S < 62μW/cm^2. No clear lower limit is able to be estimated.

15. Long-term Animal Studies:

Very few long-term animal studies involving RF/MW exposure have been carried out, largely because of their extreme difficulty and very high cost. The significant studies, also reviewed by the U.S. E.P.A., are reported here.

15.1 University of California, Berkeley:

Professor Charles Susskind and Dr Susan Prausnitz, Dept of Electrical Engineering, UC Berkeley carried out the first reported long term study for the US Air Force, Prausnitz and Susskind (1962). They exposed male Swiss albino mice to 9.27 GHz microwaves, pulsed with a 2 μs pulse at 500 Hz, 4.5 mins per day, 5 days per week for 59 weeks with an exposure level of 100 μW/cm^2. This amounts to a mean weekly exposure of 0.22μW/cm^2.

Detailed autopsies were carried out on 60 irradiated and 40 control mice who died during the experiment. Two adverse effects were more severe in the exposed compared to the control animals.

(1) Testicular degeneration (atrophy with no sperm) occurred in 40 % (23/57) of the exposed animals and 8.1 % (3/37) of the control animals.

(2) Cancer of the white cells or leukosis was seen in 35 % (21/60) of the exposed animals compared to 10 % (4/40) of the controls. This condition was described as monocytic or lymphatic organ tumours or myeloid leukaemia in the circulating blood.

At the 16-month interim kill, one month after exposure ceased, 30 % (6/20) if the exposed group had leukosis compared to 10 % (1/10) of the controls.

At the final kill at 19-months, 4 months after cessation of exposure testicular atrophy was seen in 21% (14/67) of the exposed group and 5 % (1/19) of the control group, and testicular weights were lower for the exposed group. At this stage leukosis was the same in both groups at 18 % (12/67) for the exposed group and 21 % (4/19) for the control group.

This gives an overall rate for testicular degeneration of 29.8% (39/124) for the exposed group and 7.1% (4/56) for the control group, giving a Rate Ratio of RR=4.2 . For leukosis the incidence was 26.5 % (39/147) for the exposed mice and 13.0% (9/69) for the control mice, RR = 2.04 .

These combinations of symptoms pose some challenging interpretations. Testicular degeneration is not associated with the brief heating effect of the daily exposure (4.5 mins at 100μW/cm^2), because this is usually taken to be a non-thermal exposure. The current A/NZ standard for public exposure for microwaves is 200μW/cm^2 and there is a proposal to relax it to 1000μW/cm^2, which is also claimed by those who believe that only thermal effects exists, to be harmless and non-thermal. In addition, Cairnie et al. (1980) exposed mice to microwaves at power density of 50 mW/cm^2. They found that the absorbance in the abdomen area of the liver was 11 times greater than the testes, and while the abdomen temperature was increased the testicular temperature was not.

Leukosis (the initiation of leukaemia) requires damaged DNA and chromosome aberrations which are transferred from cell to cell through mutation. The same mechanism could cause testicular degeneration. An accumulated cellular level damage mechanism is not necessarily related to the intensity but can relate to total dose in relation to rates of repair. Hence the averaging of weekly exposure is a meaningful adverse effect related level. Actual public exposure levels of 0.2μW/cm^2 and less saw childhood leukaemia incidence and death rate rises at similar exposure levels (2.74 for mortality) in the North Sydney Study.

15.2 University of Washington Case Study:

Establishment of a potential adverse human health effect can be obtained from a suitably designed and executed animal experiment. Such an experiment was carried out at the University of Washington by Professor Arthur Guy and his associates, funded by the United State Air Force. The exposed a large group of rats to pulsed radar-like microwaves, 2,450 MHz, pulsed at 800 pps, 10 μs pulse, at <0.4 W/kg, the human exposure level allowable under the ANSI standard. These rats were compared to a similar group who were sham exposed. Guy found a total of 18 malignancies in the 100 exposed rats compared to 5 in the 100 sham exposed rats, a ratio of RR=3.6 (1.34-9.70), in particular there were 9 endocrine tumours in the exposed group compared to 2 (ratio RR=4.5 (1.0-20.8)) in the control group.

On the other hand, the EPA review team worked with the original University of Washington research team, and undertook further detailed statistical analysis of their results and showed "a statistically significant elevation in the incidence of carcinomas at all sites combined."

The experiment ran for 25 months with some mice being sacrificed and analyzed at 13 months. Their initial reports concluded no effects except a significant increase in the number of benign adrenal tumours. At 13 months the exposed group had a significantly larger number of B- and T-cells than do controls, but no difference was seen at the end of 25 months. This suggests the immune system was initially disrupted, but over a 2 year period it adapted to the exposure situation. Disturbance of the immune system is also consistent with the developing cancer and tumours growth.

Table 13: Crude incidence of neoplastic lesions (Tumours)

Site/Type	Crude Tumor Incidence			
	Control		Exposed	
Adrenal Cortex	12/85	14.1 %	12/76	15.8 %
Adrenal medulla	1/73	1.4 %	7/67	10.4 %
Thyroid	9/85	10.6 %	12/76	15.8 %
Liver	1/85	1.2 %	3/76	3.9%
Pituitary	21/85	24.7 %	19/75	25.3 %
Testes	0/85	0 %	2/76	2.6 %
Epididymis	0/85	0 %	1/76	1.3 %
Pancreas	2/85	2.4 %	2/76	2.6 %
Urinary bladder	0/85	0 %	2/76	2.6 %
Stomach	4/85	4.7 %	4/76	5.3 %
Duodenum	0/85	0 %	1/76	1.3 %
Lymph node	0/85	0%	1/76	1.3 %
Soft Tissues, Thorax	0/85	0 %	2/76	2.6 %
Mesentery	0/85	0 %	2/76	2.6 %
Lymphosarcoma	3/85	3.5 %	4/76	5.3 %
Total (RR=1.35,p<0.05)	53/85	62.4 %	63/75	84.0%

These results were worrying to EPA researchers. Dr Robert McGaughy asked Dr Lawrence Kunz, the pathologist on the University of Washington study, for copies of the survival and histropathologic findings. Dr McGaughy was able to show that three statistical tests showed a statistically significant increase in carcinomas ($P<0.05$) but no statistically significant increase in sarcomas. These results are listed in Table 13.

The EPA team argue that while most chemical carcinogens affect only one or a few tissues, the distribution of the EM field as a "toxic agent" is more uniform than a "typical" chemical agent, and therefore an "all sites" approach is justified.

McGaughy et al. (1990) point to the more ubiquitous action of melatonin as an example, since,

"Nocturnal pineal melatonin activity is known to be inhibited by ELF electric fields (Wilson et al 1986) and that the pineal gland function is closely coupled to the function of other glands. Melatonin is known to inhibit tumour growth-enhancing hormones like prolactin and estrogen. The postulate has been made that when the blood melatonin concentration decreases because of the action of EM fields on the pineal gland, a tumour growth inhibitor has been reduce or effectively removed, thereby causing a stimulation of tumour growth.

Although only breast and prostate tumours have been discussed in this connection, the same regulation by melatonin might hold for other hormonally-regulated endocrine organs as well."

The Guy et al. (1985) study, along with other supporting material, led to the recommendation that the US EPA classify RF/MW as a possible human carcinogen (Class C).

The data presented in this report indicate the progressively strengthening evidence of carcinogenicity and other adverse health effects from chronic non-thermal exposure to RF/MW radiation which raise the evidence to classify RF/MW radiation as a highly probable (Class B1) carcinogen.

Note: All you need in New Zealand Law is evidence of a potential irreversible adverse environmental effect to decline this application and to recommend the identification of a site in a less sensitive receiving environment, or a potential adverse effect to require mitigation or remediation.

15.3 Polish Study:

Szmigielski et al. (1982) measured the effects of 2.45 GHz microwave radiation at 5, 10 and/or 15 mW/cm^2, 2h /day, 6 times/week exposure (average weekly exposure 360, 520 and 1,100 μW/cm^2), mice able to maintain core temperature under both exposures, specifically investigating lung cancer, breast cancer and skin cancer. Figure 26 shows the result of initiating skin tumours using 3,4 benzo-alpha-pyrene (BP) and assessing the cancer promoting effect of microwaves.

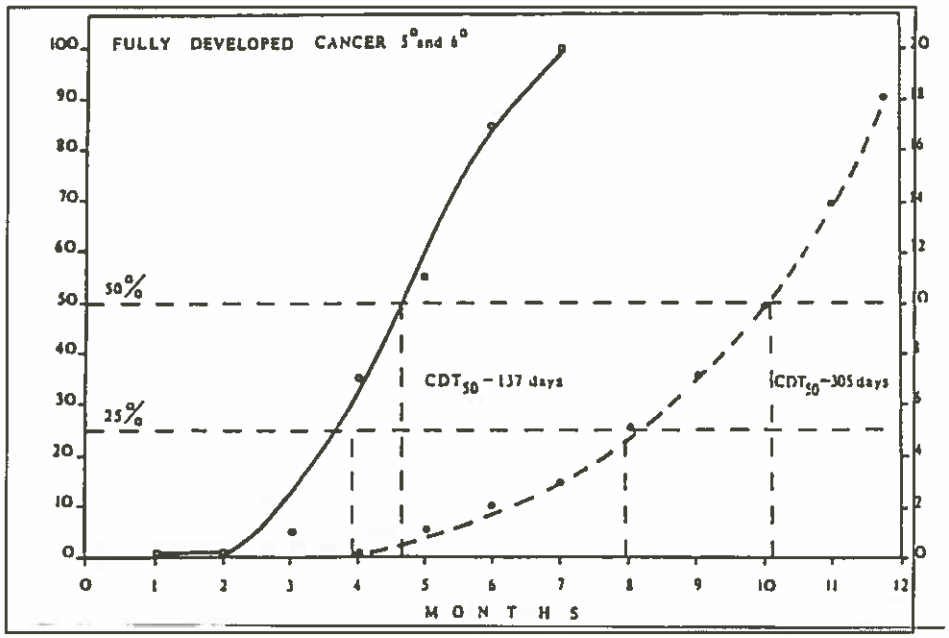

Figure 26: Growth curves of BP-induced skin tumour in mice exposed daily to 10 mW/cm^2 of 2.45 GHz microwave radiation for the whole period of tumour growth. CDT_{50} refers to the cancer development time when 50 % of the animals have tumours.

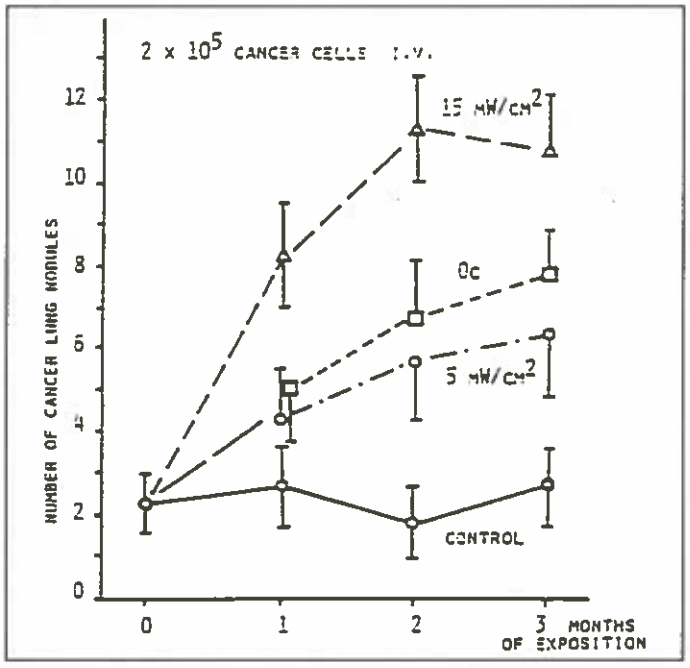

Figure 27: The number of lung tumours (following intravenous injection of 2 x 105 viable sarcoma cells) in mice exposed during 1, 2 and 3 months to 2.45 GHz microwaves (2h daily) at 5 or 15 mW/cm^2 . Oc refers to mice treated with nonspecific stress of over crowding.

Cancer development started 2 months earlier for the MW exposed mice and reached the 50 % point for the population after 137 days compared to 305 days. Hence MW significantly accelerated the growth and proliferation of skin cancer tumours.

Figure 27 shows the results of planting lung cancer (sarcoma) cells and then exposing the mice to 5 and 15 mW/cm^2 MW radiation. The 5 mW/cm^2 exposure produced an enhancement of lung cancer modules at 2.5 times more than controls after 3 months, but at a similar level to the effect of an over-crowding stress factor. The 15 mW/cm^2 exposure produced about 5.5 times more lung cancer nodules.

A parallel experiment for breast cancer for control, overcrowding stress, 5 and 15 mW/cm^2 MW exposure, the 50 % development points were 322, 255, 261 and 219 days, respectively. These show a similar relationship to the results in Figure 26 for lung cancer, except that the stress and 5 mW/cm^2 effects are reversed.

These results show statistically significant increases in numbers and rates of development of chemically initiated skin, lung and breast tumours when exposed to low level microwaves, with a significant dose response relationship in each case.

15.4 Duke University Medical Center:

Eight week old female mice were exposed to 2.45 GHz microwaves at power densities of 5 to 15 mW/cm^2 for 30 min/day over periods between 1 and 17 days, Huang and Mold (1980). Daily mean exposures were about 100 to 300 μW/cm^2, and exposure conditions were essentially isothermal. The results showed, (a) A sustained activation of tissue macrophages resulting in suppression of lymphocyte responsiveness, and (b) a gradual but temporary stimulation directed to the lymphocytes. Macrophage activation may have caused the early depression of lymphocyte responsiveness. The suppression is later overridden by the cumulative direct stimulation of lymphocytes by microwaves. Prolonged exposures is suggested to eventually result in depressed function in much the same as seen in rheumatoid arthritis which occurs from chronic immune stimulation.

They also conclude that 2.45 GHz microwaves affect the hematopoietic colony-forming abilities through altering the growth of both erythroid and myeloid cells. This is direct evidence of the ability of sub-thermal microwaves to cause chronic immuno-suppression.

15.5 Jawaharlal Nehru University Study:

Ray and Behari (1990) exposed young albino rats of both sexes to 7.5 GHz microwaves, pulsed at 1000 kHz and at a power of 600 μW/cm^2, for 3 hr /day, averaging 75μW/cm^2.

Microwave exposed rats ate and drank less and thus showed smaller weight gain. Leukocyte count increased by 35 % in the exposed animals along with a 2-fold increase in eosinophils, and Spleen, Kidney, Brain and Ovaries were significantly smaller.

15.6 Royal Adelaide Hospital Project:

Repacholi et al. (1997) exposed genetically engineered mice to a cell phone signal for 1 hr/day. This was an Australian industry funded study to allay public fears of cell phone health effects was carried out by a team led by Dr Michael Repacholi at the Royal Adelaide Hospital. In an ABC Four Corners documentary Dr Repacholi describes this study:

"We tried to get the most sensitive model of mouse that we could find that would get lymphoma and then see if we exposed them to radio frequency field, whether we could promote that cancer above its normal incidence."

Mice are often used to test toxins, chemicals and radiation effects because of the strong similarity of their cells to human cells. A search of Medline shows that since 1993 over 21100 cancer studies have used mice and 621 used tumorogenic mice.

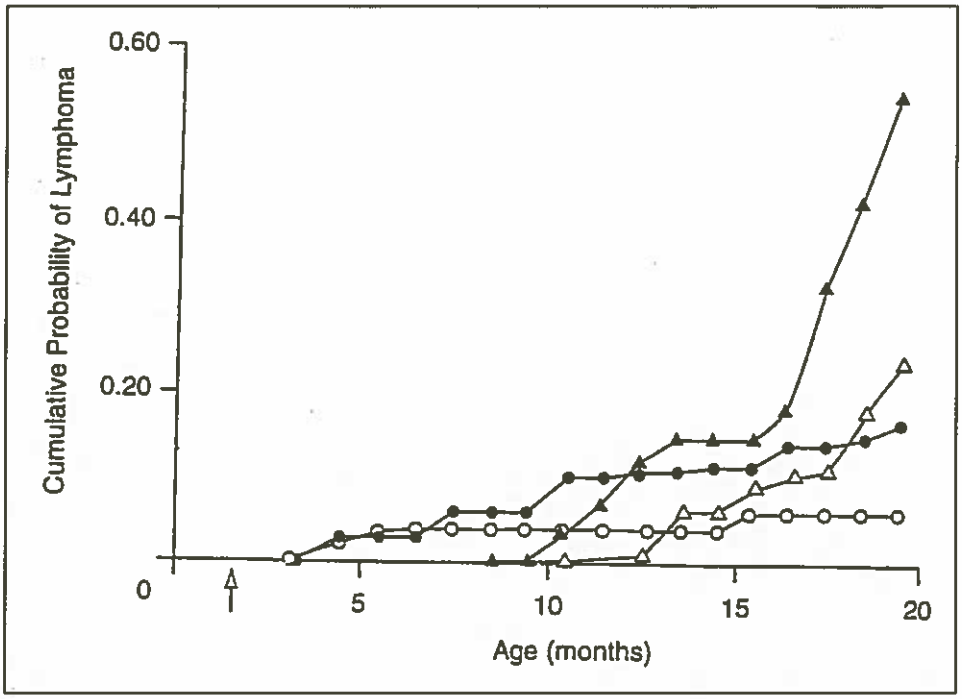

Figure 28: Rate of lymphomas increase in control and exposed groups of mice, Repacholi et al. (1997).

Their 200 genetically engineered mice normally had 22 % of them to get lymphomas in their immune system, including B-cells. About half of the mice were exposed to a moderate level of cell phone radiation for 1 hour per day for 18 months. The other half were treated the same way but not exposed. At the end of the study 43 % of the exposed mice had lymphomas. The overall Odds ratio was 2.4, p=0.006, 95% CI=1.3-4.5 . This is a highly significant results in which the cell phone radiation more than doubled the cancer rate from a 1 hour per day exposure. Mean exposure range was measured as 0.13 to 1.4 W/kg. Hence the mean daily exposure was 0.005 to 0.058 W/kg, averaging 0.03 W/kg, somewhat below the New Zealand Standard of 0.08 W/kg.

15.7 Summary and Conclusions about long-term animal experiments:

Animal experiments confirm that in mice pulsed RF/MW radiation is able to initiate statistically significantly more malignant tumours in many body organs at exposure levels assumed to be non-thermal and safe (0.4 W/kg), McGaughy (1990), and in the presence of a chemical cancer initiator to drastically increase the rate of development of lung, breast and skin cancer, Szmigielski et al. (1982), showing the strong co-promotional effects of microwave exposure. Prausnitz and Susskind (1962) found increased in testicular degeneration and increases in leukaemia at Rate Ratios and mean weekly

exposure levels which are compatible with the North Sydney Study. Cell phone radiation, Repacholi et al. (1997) enhances B-cell tumours in genetically engineered mice. These are consistent with the research summarized above on the direct mutagenic affects of RF/MW radiation and the research showing alteration of signal transduction, cell communication which influence the cellular level growth regulation and can lead to cell proliferation and thence to tumour formation and cancer.

Sub-thermal microwaves also caused significant impairment of the immune system functioning. This was recently found in people in association with powerlines (Beale at al (1997)), and recall that powerlines emit RF radiation as well as ELF fields.

16. Reproductive effects and Teratology:

16.1 Introduction:

The cellular level changes discussed and documented above are pertinent also to the consideration of potential or actual effects of RF/MW radiation on the development of human embryos, miscarriage and adverse birth outcomes.

Altered signal transduction and gap-junction communication, or DNA breakage and Chromosome Aberration in the developing human embryo is potentially damaging or fatal. Brent et al. (1993) record that 20 to 25 % of human birth defects are caused by genetic factors. Laboratory studies using mice and other animals have typically employed exposure levels in the range 10 to 100 mW/cm^2, or even higher, in the belief that the higher the dose the more likely the change of detecting a result.

The cellular processes discussed above show the fallacy of this, as does the calcium ion windowing effects, which have been monitored to change in association with environmental exposure levels of less than 10 $\mu W/cm^2$. When moderate to high exposure levels are used great care must be taken to discern between thermal effects and non-thermal effects. Real non-thermal effects can be masked by large thermal effects. The following are a sample of laboratory experiments involving mice and chickens exposed to microwaves.

16.2 Animal Studies:

Chazan et al. (1983) investigated the development of murine embryos and fetuses after irradiation with 2450 MHz microwaves. They found indications of retardation of development in the early period of gestation in mice exposed to thermal MW fields. In mice exposed to microwaves at 40 mW/cm^2 during the second half of pregnancy increased number of resorptions, stillbirths and internal hemorrhages was noted. The living fetuses had lowered body mass compared to the offsprings of sham-irradiated mice.

Berman, Carter and House (1982) found reduced weight in mice offspring after in utero exposure to 2450-MHz (CW) microwaves. They were exposed to 28 mW/cm^2 for 100 minutes daily from the 6th through 17th day of gestation. The offspring were examined either as fetuses after hysterotomy on the 18th day of gestation or as naturally born neonates on the 1st and 7th day of age. Fetuses of half of the dams were examined on the 18th day of gestation. The incidence of pregnancy and the numbers of live, dead, resorbed, and total fetuses were similar in both groups.

The mean weight was significantly lower (10%) in live microwave-irradiated fetuses, and ossification of sternal centers was significantly delayed. In the offspring that were born naturally, the mean weight of microwave-irradiated 7-day-old suckling mice was significantly lower (10%) than that of the sham-irradiated group. Survival rates of neonates in these two groups were not different. These data demonstrate that the decreased fetal weight seen in microwave-irradiated mice is retained at least 7 days after birth. Evidence from other published studies is presented to show that the retarded growth is persistent and might be interpreted as permanent stunting.

Suvorov et al. (1994) studied the biological action of physical factors in the critical periods of embryogenesis. The critical period in a chicken embryonic development (the 10-13 days of incubation) is revealed under total electromagnetic radiation. EMR is a physiologically active irritant which can influence functional state of the brain. The increased absorption of electromagnetic energy takes place in this incubation period. Its dynamics within 20 days of embryonic development has phasic, up and down character.

Electromagnetic exposure (4 hours a day) in the above mentioned period evokes a delay in embryo adaptive motor behavior (biofeedback learning). Morphological investigation shows significant pathological changes, specifically, destruction of share brain synapses. The delay in embryo hatching for a day is also detected. Radiation exposure within other periods of incubation (3-6th or 12-15th days) was not effective with respect to formation of normal motor pattern in biofeedback experiment. Unfortunately this paper is in Russian and no exposure levels are quoted in the English translation of the abstract.

Prausnitz and Susskind (1962) were not studying reproductive effects, but atrophy of the testes would have severe effects on any sperm which survived. Such sperm are unlikely to have undamaged DNA. Their exposure regime was 100 $\mu W/cm^2$ for 4.5 mins/day, averaging 0.22 $\mu W/cm^2$ /week.

16.3 Summary and conclusions about teratological animal studies:

The in utero developing embryo is very vulnerable to damage from toxins. At critical times damage to certain organs occurs. With sufficient foetal or placenta damage a spontaneous abortion is initiated. At other levels and timing of damage a still birth can result. Thermal levels of microwave exposure has produced retardation of development if exposure is in early pregnancy, and resorptions, still births and hemorrhages with exposure in the second half of the pregnancy.

A much lower microwave dose was associated with significant reduction in birth weight and permanent stunting and slowing of bone hardening. Changes in chick embryo biofeedback learning is observed and testicular atrophy was observed with a mean exposure to a radar-like signal averaging 0.22 $\mu W/cm^2$ over a week.

RF/MW radiation causes significant birth and reproductive damage in exposed animals at thermal levels and at very low short-term and extremely low average exposure levels.

17. Epidemiological Studies:

Now that we have established that there are non-thermal or athermal biological changes and observed changes in exposed animals which are consistent with possible or probable

adverse health effects, we review the epidemiological studies which find statistically significant adverse health effects in human populations, both occupational and residential.

The use and mis-use of epidmiological studies in radiation standards setting is discussed in Goldsmith (1991). He first notes that there is a tendency to use experimental studies in preference to findings from epidemiological studies. "Yet the epidemiological studies are usually the first and at time the only source of data on such critical effects such as cancer, reproductive failure and chronic cardiac and cardiovascular disease in exposed humans." A public health protection to the use of epidemiological studies is well covered by Bradford-Hill, section XX above.

Evidence published since 1990 and 1993 can extend the reviews of the U.S.E.P.A. and the W.H.O. review team. Several very recent public health studies include the North Sydney TV tower study of Hocking et al. (1996), the set of papers on the Skrunda Radar in Latvia, the analysis of the effects of the short-wave tower in Schwarzenburg, Switzerland, Altpeter et al. (1995), the U.K. study of Dolk et al. (1997a, 1997b), the brain tumour study of Grayson (1996), the mouse study of Repacholi et al (1997), and the Chinese Study of Chiang et al. (1989). These studies all have exposure measurements or calculations associated with them, which increases their power. The study by Dolk et al. (1997a, 1997b) adds confirmation to the Hocking et al. (1996) study. All of these studies show increased risk of adverse effects, on health, well-being and the environment, at mean exposure levels at a fraction of the Australian/New Zealand Standard AS 2772 (NZS 6609) and well below 2μW/cm^2.

17.1 Brief Overview of Epidemiology and RF/MW association with health effects:

It should be noted that there are many other studies which have found statistically significant increases in adverse health effects, including cancer. It is not that there is no evidence, nor even limited evidence of adverse effects. There is a large body of evidence, only part of which is reviewed here. There are sound scientific reasons for including studies involving ELF high voltage exposures (not reviewed here however), because of the similarity of cellular interations and because high voltage are a localized source of RF radiation primarily in the 3 to 30 MHz range, which is why you hear a buzz on your radio as you drive under a powerline.

The following give a brief summary of some of the published studies showing adverse effects from RF/MW effects on people.

- More neurasthenic symptoms (chronic mental and physical weakness and fatigue) in group exposed to radar (Djordevic et al., 1979).

- A major study of radar and radio exposed U.S. Navy personnel, summarized as having no reported effects, includes data which shows statistically significant increases cancer between a group assessed as high exposure compared to a group assessed as low exposure, e.g. All death (RR=1.79 (1.52-2.12)), Accidental Death (RR=2.20 (1.72-2.82)), All Diseases (RR=1.55 (1.19-2.01)), Malignant tumours (RR=1.66 (1.06-2.60)), and Lymphatic and Hematopoietic cancer (RR=2.66 (1.02-4.81)). There was also statistically increased risks of a host of illness including, Musculoskeletal, Organs of Sense, Systematic conditions, Respiratory, Cardiovascular and digestive illness, Skin, Endocrine, Neurological and Mental conditions, Robinette et al. (1980).

- Higher frequency of polycythemaemia (increase in red blood cells) with microwave exposure (Friedman, 1981).

- Swedish physiotherapists who gave birth to a deformed child or who had perinatal death had higher recorder RF/MW diathermy exposures, Kallen et al. (1982).

- Cancer incidence in the vicinity of Wichita, Kansas was found to be higher on ridges which were exposed to radar transmissions than those residents who lived in the valleys, Lester and Moore (1982 a). Residents were potentially exposed to two radars, one radar and no radars with relative cancer incidences of 470, 429 and 303 per 100,000 (1.55: 1.42 : 1.00). The association persisted through age, sex, race and socio-economic adjustments.

- Lester and Moore (1982b) found significantly higher cancer rates in U.S. counties with Air Force bases compared to those without Air Force bases, which they related to prolonged environmental exposure to RF/MW from radar.

- Association between heart disease and work with shortwave therapies, increasing with the number of treatments/week (Physiotherapists using 27 MHz diathermy) (Hamburger et al., 1983).

- Polson and Merritt (1985) criticized the analysis of Lester and Moore (1982b), pointing out weaknesses in their use of the data, such as a city could be in a country with no Air Force Base but be closer to a base in another country than a city in that county. Having made corrections for this, Lester and Moore (1985) found strengthened associations between cities and air force bases, with higher incidences of cancer related to radar transmissions.

- Lin et al. (1985) studied 951 cases of brain tumors among white male residents of Maryland during the period 1969-1982. Fifty cases of glioma and astrocytoma were observed among electrical workers exposed to EMR compared to an expected number of 18, i.e. an risk ratio of 2.8. While their exposure was mainly to ELF fields it shows the common link over a wide range of frequencies.

- Increased risk of leukaemia amongst amateur radio operators (Milham, 1985).

- In 1985 an unusual number of children with leukaemia were identified living in the vicinity of broadcasting facilities (OR = 3.4: CI=0.70 -16.41), Maskarinec et al. (1993).

- Upper limb paraesthesia and eye irritation among 30 exposed workers using 27 MHz plastic sealers (Bini et al., 1986);

- De Guire et al. (1987) report increased malignant melanoma of the skin in workers in a telecommunication industry, affecting only men, SIR = 2.7 CI : 1.31-5.02).

- Thomas et al. (1987) report a 10-fold increase in astrocytic brain tumor among electronics and repair workers employed for 20 years or more. Some risk was due to solvents, put at a factor of 2, placing RF/MW contribution at a factor of 5.

- Increased rates of paraesthesia in hands, neurasthenia and eye complaints, using 27 MHz plastic welders and sewing machines (Kolmodin-Hedman et al., 1988).

- Milham (1988) studied 67,829 amateur radio operators in Washington State and California. He concludes "The all-cause standardized mortality ratio (SMR) was 71 but a statistically significant increased mortality was seen for cancers of the other lymphatic tissues (SMR = 162), a rubric which includes multiple myeloma and non-Hodgkin's lymphomas. The all leukemia SMR was slightly but not significantly elevated (SMR = 124). However, mortality due to acute myeloid leukemia was significantly elevated (SMR = 176).

- A doubling of miscarriage rates has been reported in women working at computer terminals for more than 20 hours/week in the first three months of pregnancy (Goldhaber et al. 1988). Note that VDU's emit a wide range of RF radiation.

- Szmigielski et al. (1988) studied polish military personnel exposed to microwave radiation and reported that cancer morbidity was three times higher in the exposed group than the control group.

- Duration and severity of tonsillitis increased with combined air pollution and RF exposure (Shandala and Zvinjatskovsky, 1988);

- Electrical workers in Los Angeles county have a 4.3-fold increased risk of certain brain tumors (Preston-Martin et al. 1989).

- An increased incidence of malignant brain tumors has been reported in children of fathers exposed to electromagnetic fields and electronic solvents (Johnson and Spitz, 1989).

- Increased protein band in CSF in exposed group or radar mechanics (Nilsson et al., 1989).

- Hayes et al.(1990) report an Odds ratio for all testicular cancer of 3.1 (CI: 1.4-6.9) for a small sample of workers who were occupationally exposed to RF/MW radiation.

- U.S. Navy electrician's mates have an excess risk of leukaemia, RR=2.4 (1.0-5.0), Garland et al. (1990)

- W Shao-Guang, et al. (1990) reports a Chinese study which found a significant increase in neurasthenic syndrome backed up by blood biochemical changes.

- Savitz and Chen (1990) show significant increased risk of childhood cancer (Neuroblastoma (OR=11.8*), Brain Tumour (OR=2.7*) and CNS tumors (OR=1.7)) associated with parents who work in electrical and electronic industries.

- Danish physiotherapists working with shortwave diathermy, who were "highly exposed" to RF, only 17% of newborn infants were boys, and exposure was associated with stillbirth/death within a year, prematurity and low birth weight, Larsen et al. (1991).

- Increased risk for all brain tumours (RR=2.9 (1.2-5.9)) and glioblastomas (RR=3.4 (1.1-8.0)) for assemblers, and repairmen in the radio and TV industry, Tornqvist et al. (1991)

- Microwave heating reduces immune system factors in human breast milk, compared to conventional heating. Microwave heating significantly reduces the IgA for E coli bacteria, producing five times more E coli for 25 °C heating and 18 times more after 3 hours for 98°C heating, Quan et al. (1992).

- United States physical therapists (Ouellet-Hellstrom and Stewart (1993)) show a 1.59-fold increase in miscarriage in the first 7 weeks of gestation when using microwave diathermy, and a dose-response relationship with increased treatments/month.

- Goldsmith (1995) reports an up-dated analysis of the US embassy in Moscow which does show a significant elevated risk of a wide range of adult cancers, and including childhood leukaemia, after years of microwave irradiation, exposed to average levels of radar produced microwaves of long-term average indoor exposure of 0.2 to 0.5 $\mu W/cm^2$, daily peaks between 5 and 18 $\mu W/cm^2$ on the outside walls.

- Increased risk of female breast cancer with exposure to radiofrequency EMF, RR=1.15 (1.1-1.2), Cantor et al. (1995).

- Altpeter et al (1995) studied populations living near and further away from a shortwave transmitter in Schwarzenburg, Switzerland. The statistically elevated symptoms in the high and medium exposure groups, compared to the low exposure group, include Nervosity and restlessness, Disturbances in falling asleep and difficulty in maintaining sleep, Joint pains, Psychovegetative Index changes, Disturbances of Concentration, General Weakness and Tiredness, Constipation, Diarrhea and Lower back pain, all significant at $p<0.02$ except the first for which $p=0.034$ which is less than the usual significance level of $p<0.05$. Children's advancement from primary school to secondary school was significantly slower in the exposed group. They conclude that even though the association is weakened by a small sample size, an adverse effect from the transmitter "cannot be excluded".

An increased exposure from 1 mA/m to 10 mA/m ($0.038\mu W/cm^2$ to $3.8\mu W/cm^2$) had on Odds Ratio for insomnia of 1.13 (CI: 1.04-1.23) and from 0.1 mA/m to 1 mA/m ($0.00038\mu W/cm^2$ to $0.038\mu W/cm^2$), OR=2.1 (CI: 0.95-4.57). Table 7 presents the adjusted Odds Ratios for the primary effects found, which show significant dose response relationships and a highly statistically significant increase with mean exposure increase.

Table 14: Odds Ratios for an increase in 24-hour average exposure from 1 mA/m (0.04 $\mu W/cm^2$) to 10 mA/m (3.8 $\mu W/cm^2$) adjusted for age, sex, attribution, and duration of time lived at the same place.

Symptoms	OR	95% Conf. Interval
Nervosity	2.77	1.62-4.74
Diff. in falling asleep	3.35	1.86-6.03
Diff. in maintaining sleep	3.19	1.84-5.52
Joint Pain	2.46	1.37-4.43
Limb Pain	2.51	1.15-5.50
Cough and Sputum	2.80	1.18-6.64

- Hocking and Gordon (1996) found a 2.74-fold increase in childhood leukaemia death within 4 km of TV and FM radio transmission masts in North Sydney between 1972 and 1990. Mean exposures were measured in the range 0.04 to 0.4 $\mu W/cm^2$.

- Polish Military personnel (1971-85) exposed to above average radar and radio sourced RF/MW show large increases in leukaemia (Lymphoma: RR=5.8 (2.11-9.74); Chronic lymphacytic: RR=3.7 (1.45-5.18); Acute Lymphoblastic: RR=5.8 (1.22-18.16); Chronic myelocytic: RR=13.9 (6.72-22.12); Acute myeloblastic: RR=8.6 (3.54-13.67) and Total: RR=6.31 (3.12-14.32). Also show statistically significant associations for cancer of the esophagus and stomach, colorectal, skin (including melanomas), CNS and brain. (Szmigielski , 1996)

- U.S. Air Force personnel showed increased incidence of brain tumour with exposure to ELF (RR=1.28 (0.95-1.74)), and RF/MW (RR=1.39 (1.01-1.90)).

- The Skrunda Radar provides a living laboratory for the chronic low level effects of exposure to RF/MW radiation. To date investigations have revealed a number of statistically significant changes associated with exposure to the radar signal. These include:

  Impaired scholastic performance of children in the open field exposure range of 0.0008-0.41 $\mu W/cm^2$, mean measured level in the range 0.0028- 0.039$\mu W/cm^2$.

  A 6-fold increase in broken chromosomes in the peripheral erythrocytes of the exposed cows ($p<0.01$). for a measured exposure would be in the range 0.042 to 6.6$\mu W/cm^2$, mean exposures in the range 0.157 to 0.63$\mu W/cm^2$.

  A statistically significant ($P<0.01$) negative correlation between the relative additional increment in tree growth and the intensity of the electric field. The Pine trees at 4 km were exposed to a range of 0.011 to 0.41$\mu W/cm^2$, a mean open field exposure of 0.039$\mu W/cm^2$ and measured distance exposure of 0.0027$\mu W/cm^2$ (for the radar signal). A probable biological mechanism was identified through observed changes in physiological conditions.

  Chromosome and reproductive damage in plants exposed RF/MW in the range 0.042 to 6.6$\mu W/cm^2$.

  Chronic exposure to pulsed RF radar signals is associated with chromosome damage in plants and animals, with associated reproductive aberration in plants, and growth reduction in pine trees linked to observed physiological changes, and scholastic impairment of school children occurs in relation to exposure levels which fall well below 2$\mu W/cm^2$, below 0.1$\mu W/cm^2$. and even below 0.01$\mu W/cm^2$.

- Dolk et al. (1997 a, b) found small but significant increases in adult leukaemia, which decreases with distance from the transmitter, associated with 21 FM and TV transmission towers in the United Kingdom. This is a strong dose-response result.

Study after study shows cancer and other health problems associated with RF/MW exposure. This shows why independent scientists continually find it disturbing and unprofessional when government and international reviews, such as that carried out for

the WHO, Repacholi (1993) publish conclusions which are weak or even misleading, by stating that there is "***no clear evidence of detrimental effect***". This is strongly at odds with the data presented.

When asked whether epidemiological evidence on the adverse health effects of RF/MW could be only described as a "weak link", Professor Goldsmith replied (p137, line 36)

> **"I disagree. I think when children die of cancer between 5 and 18 $\mu W/cm^2$ over a period of time - exposure is not weak. It is significant."**

Here Professor Goldsmith is referring to the children of the staff of the U.S. Embassy in Moscow and other Eastern European embassies and the range of peak exposure levels on the outside walls of the United States Embassy in Moscow. The daily mean external wall exposure was in the range 1.0 to 2.4$\mu W/cm^2$, internal exposure being less than 0.2 to 0.5$\mu W/cm^2$.

17.2 Occupational Studies:

17.2.1 U.S. Physiotherapists Spontaneous Miscarriage Study:

17.2.1.1 The Study:

Ouellet-Hellstrom and Stewart (1993) carried out the largest study of physiotherapists in relation to early (first trimester) spontaneous miscarriage associated with expose to shortwave and microwave leakage fields from diathermy equipment. In a sample of 11,598 pregnant physiotherapists in the U.S., 6684 reported having ever used microwave or shortwave diathermy, 1791 of whom had experienced early spontaneous miscarriage. From these a case group (miscarriage) was selected for a microwave exposed group and a shortwave exposed group.

Table 15: Unconditional odds ratios for the association between risk of recognised miscarriage and reported exposure to microwave diathermy during the 6 months prior to and the first trimester of pregnancy: Physical Therapists Study, 1989-1990.

	No. of exposures	Case pregnancies	Control pregnancies	OR*(95% CI)	χ^2 test for trend
All pregnancies	0	1,459	1,494	1.00	
	<5	88	86	1.05 (0.77-1.43)	
	5-20	72	49	1.50 (1.04-2.17)	
	>20	45	29	1.59 (0.99-2.55)	
p>0.005					
	Total no.	209	167	1.28 (1.02-1.59)	
No prior fetal loss	0	1,102	1,258	1.00	
	<5	71	76	1.07 (0.78-1.49)	
	5-20	58	47	1.41 (0.95-2.09)	

	>20	34	25	1.55 (0.92-2.61)
p>0.01				
	Total no.	167	151	1.26 (1.00-1.59)

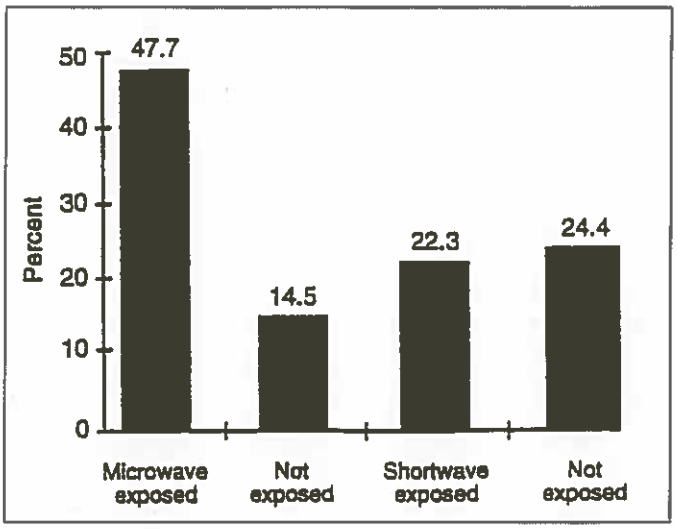

Figure 29: Proportion of miscarriages occurring before the seventh week of gestation, by exposure status, Ouellet-Hellstrom and Stewart (1993).

Each person in these groups was matched with a control (pregnancy) person from the "ever exposed" group of 6684, making up a nested case-control study. These groups were then compared relative to their exposures in the six months prior to the pregnancy and in the first trimester.

An excess of miscarriages was found for microwave exposure (OR=1.28; CI: 1.02-1.59), with a statistically significant dose-response relationship ($p<0.005$), but no excess was found for shortwave exposure. In addition, of those miscarriages occurring in association which microwaves, 47.7% occurred before the 7th week of gestation, whereas only 14.5% of the unexposed miscarriages occurred in that period. Hence microwave exposure is highly related to accelerated early miscarriage but shortwave exposure isn't. Other studies, Kallen et al. (1982) for example, found shortwave exposure was associated with perinatal death and congenital deformity.

17.2.1.2 Types of Biological Mechanisms:

Two possible types of biological mechanisms have been proposed to explain this associated effect of microwaves and early spontaneous miscarriage. The first, favoured by the National Radiation Laboratory (NZ) and the Australian Radiation Laboratory staff, is a thermal mechanism, such as the production of heat lesions in the placenta and/or foetus, causing damage and subsequent miscarriage. This requires a significant temperature rise in the affected tissue. The second involves cumulative mutational DNA and aberrated chromosomes, probably involving enhanced free radicals. This mechanism is suggested by observations of aberrated chromosomes in blood analysis of people exposed to microwaves from radar, Garaj-Vrhovac and Fucic (1993).

17.2.1.3 The Heating Issue:

The key to resolving this is the ability of the known exposure regime to produce significant foetal heating or not. The highest exposure at 15 cm from the pads is 15 mW/cm^2, while the top of the usual range is 1,200 μW/cm^2. Hocking and Joyner (1995) in their criticism of the paper, suggest that the result is implausible because shortwaves penetrate the foetus much more easily than do microwaves. Hocking and Joyner use a model developed by Telecom Australia to show that for a frontal exposure of 1000 μW/cm^2, the maximum SAR in the uterus is 0.209 W/kg for 27.12 MHz, 0.023 W/kg for 915 MHz and 0.000027 W/kg for 2,450 MHz. For the maximum conceivable exposure (15 mW/cm^2), the 915 MHz and 2,450 MHz SARs would be 0.345 W/kg and 0.00041 W/kg , respectively.

Ouellet-Hellstrom and Stewart (1995) in reply to Hocking and Joyner's comments state:

> **"We disagree with the general scientific view of Hocking and Joyner as expressed in their closing statement. In general, one should examine the extent to which competing explanations are supported by the data, not whether the data is supported by the explanations. The data are fixed, but the explanations are not."**

For normal blood flow the temperature rise rate at 4 W/kg is about 0.02 °C/min at 20 °C and 50 % RH, Adair (1993). This gives a 1 °C rise after 50 minutes. At 0.345 W/kg the heating rate will be about 0.0017°C/min. Hence a 2 to 5 minute exposure at the maximum conceivable rate would result in a foetal temperature rise of 0.004 to 0.009°C. This is far too low to cause thermal lesions and therefore rules this out as a possible mechanism.

17.2.1.4 Biologically Plausible Mechanism:

Electromagnetically reduced melatonin could be related to spontaneous abortion. According to Sandyk et al.(1992):

> **"The causes of spontaneous abortion can be divided into two main categories: those arising from chromosomal anomalies and those arising from abnormalities in the intrauterine environment. In the following communication, we propose that deficient pineal melatonin functions in early pregnancy may be causally related to the development of spontaneous abortions in cases where chromosomal anomalies or structural abnormalities of the uterus have been excluded."**

Microwaves are shown to be associated with DNA breakage in rats brains, Lai and Singh (1995, 1996) and to cause chromosome aberrations in living humans blood, Garaj-Vrhovac and Fucic (1993), and hence can produce the first cause of spontaneous abortion. Reduced melatonin allows greater concentrations of free radicals to exist. These damage the DNA and chromosomes, leading to a similar mechanism for miscarriage of the deformed foetus.

Therefore, thermal shock and cumulative buildup of thermal lesions is implausible and cumulative cell damage, including melatonin mediated free radical chromosome damage is a highly plausible mechanism.

Thus, it is appropriate to estimate the risk of spontaneous miscarriage in terms of monthly mean exposure since the dose-response relationship is expressed in terms of treatments

per month. A significant occupational exposure will only occur then, if many treatments are given and the operator stands very close to the equipment for prolonged periods. Assuming a conservatively long estimate of 2 minutes exposure per treatment, the dosage per treatment is 0.01 to 0.144 J/cm^2.

17.2.1.5 Microwave dose associated with the risk:

One treatment per month is in the range 0.004 to 0.056 μW/cm^2, mean 0.03 μW/cm^2; 10 per month 0.04 to 0.56 μW/cm^2 , mean 0.3 μW/cm^2; and 20 treatments per month 0.08 to 1.11μW/cm^2, mean 0.6 μW/cm^2. The lowest limit is very difficult to estimate with reliability but the mean level of the middle band is 0.3 μW/cm^2. This suggests that a 20 to 50% increase in miscarriage occurred with a mean monthly microwave exposure of somewhat less than 0.5 μW/cm^2.

17.2.1.6 Relevance to mobile phone base stations:

The fact that this level of microwave exposure is found near base stations and that there are currently no documented reports of increased incidence of miscarriage occurring near cell sites is not surprising nor a proof that the hypothesis advanced here is wrong. It simply results from the fact that nobody reports or records miscarriage. Several other factors exists. Miscarriage is not reported and no statistics are being collected. Each pregnant woman can only miscarriage once per child, with a several month wait until the next pregnancy. Each spontaneous miscarriage is isolated and does not form a pattern. Many causes are possible. Very few miscarriages are investigated, unless it becomes an issue from a cluster pattern and then a medical or environmental cause is sought. Few pregnant people live near mobile phone base stations. However with the unrestricted siting policy advocated by the companies and accepted by almost all councils, this is changing significantly month by month.

Increased incidence of miscarriage is potentially occurring right now and until it is scientifically assessed, we will not be able to rule out the scientifically indicated probability. It remains a potential adverse effect under the definitions of the Resource Management Act 1991. The studies presented here give ample grounds for requiring the siting of cell sites far enough away from residences to avoid an increase in risk through sections 5 and 3 of the Act.

A statistically significant 50 % increase in miscarriage risk was identified with 5 to 20 treatments per month. Taking the typical number in this range as 10 treatments per month the mean exposure is in the range 0.04 to 0.56 μW/cm^2 . A public exposure limit of 0.1 μW/cm^2 should be adopted until the effect was conclusively show to occur at or below this level, or not at all.

17.2.2 Korean War U.S. Navy Study:

Robinette et al. (1980) was quoted by Dr Michael Repacholi in evidence for BellSouth, following the conclusions stated in the original paper, as showing no effects from exposure to radio and RF/MW radiation. This comes from taking the authors' conclusions and not looking at the data itself. Doubt was thrown on these conclusions at the hearing by Professor of Epidemiology, Dr John Goldsmith on the basis of published comments from Dr Charlotte Silverman, a leading epidemiologist and co-author of the original paper when she said in relation to the results of this study, Silverman (1979), "while some

significant differences among the occupational groups classified by level of potential exposure have been found with respect to all end points studied, the differences could not be interpreted as a direct result of microwave exposure." Professor Goldsmith was clearly stating that Dr Silverman had concluded that significant differences has been found in all studied end points, and that this was at variance with the conclusions of the 1980 paper.

Robinette et al. (1980) acknowledge the strong possibility of mis-classification of exposure hazard. They carried out a survey of the assumed high exposure groups and a hazard number was allocated to each. Electronics Technicians (ET) were 1620, Fire Control Technicians (FT) were 2870 and Aviation Electronics Technicians were 3700. Hence a low versus high exposure comparison can be made taking the incidence ratio (Risk Ratio) between ET and AT, Table 16.

This analysis is much more consistent with Dr Silverman's conclusions reported in the 1979 conference paper, Silverman (1979). It is also consistent with the substance of the material in the original paper.

Table16: Mortality Incidence per 1000 and Risk Ratio (AT/ET) as an indication of the high exposure (AT) to low exposure (ET) difference.

Causes of Death	Low	High	Risk Ratio	95 % CI
All Deaths	33.7	60.5	1.79	1.52 - 2.12
Accidental Death	13.5	29.6	2.20	1.72 - 2.82
Motor Vehicle Death	6.3	6.1	0.97	0.60 - 1.59
Suicide, Homicide, Trauma	4.4	6.1	1.38	0.83 - 2.29
Suicide	3.4	2.7	0.80	0.39 - 1.63
All Diseases	15.2	23.5	1.55	1.19 - 2.01
Malignant Neoplasms	5.0	8.2	1.66	1.06 - 2.60
Digestive and Peritoneum	1.1	1.2	1.07	0.35 - 3.21
Respiratory	1.2	2.1	1.75	0.72 - 4.25
Eye, Brain, CNS (FT/ET)	0.4	0.9	2.40	0.57 - 10.03
Skin	0.2	0.6	2.66	0.45 - 15.94
Lymphatic and Hematopoietic	1.4	3.1	2.22	1.02 - 4.81
Circulatory System Disease	7.6	9.5	1.24	0.83 - 1.85
Digestive System Disease	0.8	2.7	3.27	1.35 - 7.89
Other Diseases	1.6	2.7	1.71	0.78 - 3.74

In that the original data shows a significant increase in mortality risk for the high exposure group, the stated conclusion in the abstract of the paper is **clearly wrong and misleading** when it states:

> **"No adverse effects were detected in these indices that could be attributed to potential microwave radiation exposures during the period 1950-54."**

Adverse effects are even more clear with a consideration of the morbidity data derived from men receiving VA compensation for treatment, Table 12 from Robinette et al. (1980).

Robinette et al. (1980) stress that while considering the data about death, other disease would have been present which would not be reported:

"Further, it is possible that effects involving cardiovascular, endocrine and central nervous system do exist, but are transient, disappearing with the termination of exposure or soon thereafter, or are not perceived to be sufficiently consequential to result in admission to hospital."

Morbidity effects were investigated using VA compensation claims. The average exposure of the FT+AT group is 3286. Table 10 is extracted from the data in Table 12 in Robinette et al. (1980). Table 17 shows that sickness was considerably higher amongst the highly exposed group compared with the low exposure (ET) group. The following have Risk Ratios elevated by 30 % or more: Musculoskeletal (RR = 1.93), Organs of special sense (RR = 1.62), Systematic conditions (RR = 3.5), Respiratory (RR = 1.74), Cardiovascular (RR = 2.03), Digestive (RR= 1.37), Skin (RR = 1.30), Endocrine (RR = 1.45), Neurological (RR = 1.44), and Mental Conditions (RR = 1.67).

Table 17: Number of men receiving VA compensation and pension, December 1976 and rates per 1000 men per year by diagnosis and exposure class, and Risk Ratio (FT+AT)/ET.

	ET		FT+AT		Risk Ratio	
Mean Hazard Index	1620		3286			
	No.	Rate	No.	Rate	RR	95% CI
Diagnosis:						
Musculoskeletal	115	8.8	119	16.9	1.93	1.69-2.20
Organs of special sense	49	3.7	42	6.0	1.62	1.31-2.00
Systematic conditions	3	0.2	5	0.7	3.50	1.69-7.26
Respiratory	55	4.2	51	7.3	1.74	1.43-2.11
Cardiovascular	43	3.3	47	6.7	2.03	1.64-2.51
Digestive	74	5.7	55	7.8	1.37	1.15-1.64
Genitourinary	31	2.4	10	2.7	1.13	0.79-1.63
Skin	83	6.3	58	8.2	1.30	1.10-1.54
Endocrine	15	1.1	11	1.6	1.45	0.97-2.16
Neurological	21	1.6	16	2.3	1.44	1.03-2.01
Nerves	15	1.1	3	0.4	0.36	0.19-0.68
Mental Conditions	51	3.9	46	6.5	1.67	1.36-2.05

Note that the Risk Ratios in Table 6 are smaller than they would be if AT was compared with ET, and the "high exposure" group was not diluted by including FT.

A part of the Respiratory disease and Cardiovascular Disease increase could be attributable to increased incidence of smoking. However these do not account for all of the increase in these diseases, nor of the wide range of disease increase detected.

Note also that the reference group, ET, have an elevated Hazard Number compared to other servicemen and considerably elevated compared to the general public. Hence the Risk Ratios are quite large underestimates of the effect of increased chronic exposure to microwaves emitted by radar.

Dr Ruey Lin of the Maryland Department of Health, Lin (1985) reviewed this study and concluded that the exposed and control groups were in fact both exposed groups, leading to an under-estimate of the identified effects.

Since all of the subjects are acknowledged to have some radar exposure on a regular basis, such as when they are on deck, it is relevant to compare the incidence of mortality of the servicemen with a large group of unexposed men. Cancer mortality statistics are available for New Zealand men. Since rates of cancer death rise with age a well define age cohort is necessary.

As of 1952, 88.7% of the studied service men were 25 or younger. Mortality analysis covered the period to 1974 making around 89% being 47 years old or less. The standardized mortality for death from cancer for all causes of cancer in Males in New Zealand in the 25 to 49 age group is 2.21 per 1000. All of the Korean War veterans have a far higher rate than this and all would have been exposed to more radar signals than the New Zealand population. Even the lowest rate for Radiomen at 4.21/1000 is 1.9 times higher than the New Zealand age adjusted male all cancer rate. The highest rate for Aviation Electronics Technicians (8.25/1000) is 3.73 times higher.

17.2.3 Polish Military Study:

The Polish Military Study, Szmigielski et al. (1988) reported significant health effects from chronic RF/MW exposure but did not have exposure estimates associated with it. Analysis of the exposure regime described allows an annual mean career range of exposure to be estimated with a degree of reliability because of the hygiene regime which was in place and measurements which were made. Another 5 years of data has now been added and reported, Szmigielski (1996).

17.2.3.1 Background:

Szmigielski et al. (1988) carried out an extensive retrospective study of Polish Military personnel with radar exposure, covering a longer period to allow for the latency of cancers. This was updated to extend the period involving cancer morbidy to between 1971 and 1985, Szmigielski (1996). The mean annual population was 128,000 with around 3700 (3%) being considered to occupationally exposed to RF/MW. In this group statistically significant increases in many forms of cancer were detected, consistent with the Moscow study below. No analysis of the exposure regime was presented to the Planning Tribunal. While it was impossible to assign an exposure to each individual, the exposure regime was extensively studied and it is possible to make an estimate of the likely career mean range of exposure for those with very high exposures, setting the likely maximum exposure range for the effects identified.

17.2.3.2 Exposure Assessment:

Szmigielski (1996) states that the exposure regime was considerably more uniform than most exposures because of exposure hygiene controls and reporting of high exposures. Szmigielski (1988) describes the daily exposures as 4-8 hours below 200$\mu W/cm^2$ with several minutes in the range 200-1000$\mu W/cm^2$. Incidents of short-lasting exposures estimated up to 10-20 mW/cm^2 were reported but were more frequent before 1960 when the hygiene controls were introduced.

Exposures were extensively measured by military safety groups, with the finding that 80%-85% of the posts were in the 10-200$\mu W/cm^2$ range, and 15 % in the 200-600$\mu W/cm^2$ range, and where EM fields mostly pulse-modulated RF/MWs at 150 to 3500 MHz. Safety rules limiting exposure were established in 1961 and are outlined in Table 18.

A highly exposed person would spend most of the working day in Zone 2, a small number of hours in Zone 3 and a few minutes in Zone 4 at most, since a person in a highly exposed occupation was generally required to follow hygiene principles set out in the Standard. About 16 hour/working day would be spent away from the occupational exposure zone. Hence the maximum exposure regime is suggested in Table 18.

Because the exposure distribution is skewed, the mean and median exposures are closer to the lower bound of the range. From Tell and Mantiply (1980), the distribution of population exposures in major US cities, the mean is 0.01$\mu W/cm^2$ and the 15 percentile is 0.069$\mu W/cm^2$. Hence the ratio of the upper 15 percentile to the mean is 0.153. Applying this factor to the upper limit of each exposure class gives an approximate estimate of the mean exposure.

Table 18: Polish Occupational exposure standards (Czerski (1985)) for RF/MW exposure, 300 MHz - 300 GHz. Exposure in $\mu W/cm^2$

Zone	Stationary Antennae	Rotating antennae
1) Safe, Human occupancy unrestricted	< 10	< 100
2) Intermediate, access limited to authorized personnel, occupational exposure permissible during work shift.	10 - 200	100 - 1000
3) Hazardous, access limited to authorized personnel, duration of exposure (t in hrs) defined by the formula in parentheses.	200 - 10,000	1,000 - 10,000
(p in W/m^2: 1 W/m^2 = 100$\mu W/cm^2$)	($t=32/p^2$)	($t=800/p^2$)
4) Danger Zone, human occupancy prohibited.	> 10,000	> 10,000

Table 19: Estimated maximum average daily career exposure scenario for a very highly exposed serviceman.

Zone classification and safety limits	Daily Time	%
Danger Zone (>10,000$\mu W/cm^2$, average 15,000$\mu W/cm^2$)	1 minutes	37.4
Hazard Zone (200-10,000 $\mu W/cm^2$, average 2750 $\mu W/cm^2$)	5 minutes	34.4
Intermediate Zone (10-200 $\mu W/cm^2$, average 30.6 $\mu W/cm^2$)	6 hours	27.5
Safety Zone (<10 $\mu W/cm^2$, average 1.5 $\mu W/cm^2$)	1.9 hours	0.4
Residential (<1 $\mu W/cm^2$, average 0.153 $\mu W/cm^2$)	16 hours	0.4

The regime in Table 19 gives a high exposure workday mean of 27.8$\mu W/cm^2$, and a working week average of 19.9 $\mu W/cm^2$, and an annual average (assuming 46 working

weeks) of 17.6 $\mu W/cm^2$. This is 1760 times higher than the mean U.S. urban exposure of 0.01 $\mu W/cm^2$. The residential exposure in Table 12 (0.153$\mu W/cm^2$) is over 15 times higher than the U.S. urban mean. This is appropriate because most servicemen live on or near the military base and hence are exposed to radar signals. Lester and Moore (1985) found increased cancer rates in cities adjacent to air force bases. It is unlikely that a serviceman would be in this highly exposed regime for all of their career and so long-term mean maximum exposures are likely to be less than this, say 40-80 %. Using the extremes of each of these gives the range 7-14 $\mu W/cm^2$ for the career maximum average exposure for Polish servicemen.

17.2.3.3 Summary of Health effects:

Prof. Szmigielski has published the health effects data in two parts, Szmigielski (1988) and Szmigielski (1996), the first covering the period 1971 to 1980 and the second 1971-1985. Szmigielski (1988) reached the following conclusions:

> **"In summary, from a retrospective study that covered a large, well controlled population with a known population of subjects, and that has a relatively long period of observation (1971-1980) the following conclusions can be drawn:**
>
> - **The risk of developing clinically detectable neoplastic disease was about 3 times higher for the personnel exposed occupationally to MW/RF radiation. The higher risk appeared for malignancies originating from hemato-lymphatic systems (morbidity about 7 times higher). Other more frequent neoplasms were located in the alimentary tract and in skin (including melanomas).**
> - **The highest risk factor of cancer morbidity related to occupational exposure to MW/RFs appeared for subjects at the age of 40-49 who had a 5-15 year period of exposure.**
> - **Morbidity rates of neoplasms in personnel exposed occupationally to MW/RFs showed a strong correlation with the period of exposure.**
> - **Neoplasms (cancer tumors) of the same localization and/or type developed earlier (by about 10 years) in personnel exposed occupationally to MW/RFs than in those not working in the MW/RF environment.**

The extension to 15 years of data was reported in Szmigielski (1996). The results are in Tables 20,21 and 22.

Table 20: Incidence of haemopoietic and lymphatic malignancies (per 100,000 subjects annually) in military personnel exposed and non-exposed (control) to radiofrequency and microwave radiation.

Type of malignancy	Incidence	Incidence	RR	95 % Confid.	Significance
	Non-exposed	Exposed			
Hodgkin's disease	1.73	5.12	2.96	1.32 - 4.37	<0.05
Lymphoma (non-Hodgkin and lymphosarcoma	1.82	10.65	5.82	2.11 - 9.74	<0.001
Chronic lymphacytic leukaemia	1.37	5.04	3.68	1.45 - 5.18	<0.01
Acute lymphoblastic leukaemia	0.32	1.84	5.75	1.22 - 18.16	<0.05

Chronic myelocytic leukaemia	0.88	12.23	13.90	6.72 - 22.12	<0.001
Acute myeloblastic leukaemia	0.71	6.12	8.62	3.54 - 13.67	<0.001
Total	6.83	43.12	6.31	3.12 - 14.32	<0.001

Table 21: Incidence of neoplasms (tumors) (per 100,000 subjects annually) in age groups of military personnel exposed and non-exposed (control) to radiofrequency and microwave radiation, Szmigielski (1996).

Age Group	Incidence		Incidence	OR 95 % Confidence	Significance
	Non-exposed	Exposed		limits	(p-value)
All sites:					
20-29	11.62	21.11	2.33	1.23 - 3.12	<0.05
30-39	18.37	42.28	2.30	1.04 - 3.06	<0.05
40-49	84.29	161.62	1.92	0.98 - 2.84	<0.05
50-59	186.71	274.13	1.47	0.92 - 2.21	N.S.
All Ages	57.6	119.12	2.07	1.12 - 3.58	<0.05
Haemopoietic/lymphatic malignancies					
20-29	2.12	17.30	8.16	3.11 - 22.64	<0.01
30-39	3.08	26.43	8.58	3.46 - 19.58	<0.01
40-49	8.32	73.25	8.80	4.13 - 15.27	<0.01
50-59	24.13	108.62	4.47	2.56 - 6.81	<0.01
All ages	6.83	43.12	6.31	3.12 - 14.13	<0.001

Table 22: Incidence of neoplasms (per 100,000 subjects annually) in military personnel exposed and non-exposed (control) to radiofrequency and microwave radiation, Szmigielski (1996).

Localization of malignancies	Incidence (Expected)	Incidence (Exposed)	Risk Ratio	95% CI limits	p-value
Pharynx	1.96	2.12	1.08	0.82-1.24	N.S.
Esophageal and stomach	4.83	15.64	3.24	1.85-5.06	<0.01
Colorectal	3.96	12.65	3.19	1.54-6.18	<0.01
Liver, pancreas	2.43	3.58	1.47	0.76-3.02	N.S.
Laryngeal, lung	21.89	23.26	1.06	0.72-1.56	N.S.
Skin, including melanomas	3.28	5.46	1.67	0.92-4.13	<0.05
Nervous system including brain tumour	2.28	4.36	1.91	1.08-3.47	<0.05
Thyroid	1.38	2.12	1.54	0.82-2.59	N.S.
Haematopoietic system and lymphatic organs	6.83	43.12	6.31	3.12-14.32	<0.001
All malignancies	57.60	119.12	2.07	1.12-3.58	<0.05