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Table 1. Studies of EMF Stimulation of DNA and Protein Synthesis (page 1)

Table 1 summarizes both ELF and RF studies (mainly frequencies 50Hz, 60Hz, 900MHz, 1.8GHz) relevant to stimulation of DNA and stress protein synthesis in many different cells.

Study/Journal	Frequency	Cells/effect on hsps
Balcer-Kubicek et al, 1996 Radiation Res	60Hz	HL60 **NO** synthesis of myc
Blank et al, 1994 Bioelectrochem Bioenerg	60Hz	*Sciara* salivary glands [temperature, EMF, cause same new proteins]
Capri et al, 2004 Int J Radiat Biol	1800MHz	monocytes **NO** effect on apoptosis, hsp70
Caraglia et al, 2005 J Cell Physiol	1.95GHz	epidermoid cancer cells Induces apoptosis, hsp70
Chauhan et al, 2006 Radiation Res	1.9GHz	human lymphoblastoma (TK6) **NO** hsp response
Chauhan et al, 2006 Int J Radiat Biol	1.9GHz	two human immune cell-lines HL60,MM6 **NO** hsp response
Cleary et al, 1997 Bioelectromagnetics	27MHz	HeLa, CHO (also at 2450MHz mammalian cells **NO** hsp after 2 hr exposure, 24 hr to measurement
Chow and Tung, 2000 FEBS Letters	50Hz	E. coli strain XL-1 BLUE + plasmid pUCB DNA repair improved
Czyz et al, 2004 Bioelectromagnetics	modulated 1.71GHz	p53-deficient embryonic stem cells hsp70 expression, but not in wild type

Table 1. Studies of EMF Stimulation of DNA and Protein Synthesis
(page 2)

Daniells et al, 1998 Mutat Res	750MHz	C elegans induced hsp16
Dawe et al, 2005 Bioelectromagnetics	750MHz	C elegans (same lab as above paper) hsp 16 may be due to temperature rise
Di Carlo et al, 2002 J Cell Biochem	60Hz	chick embryo repeated EMF causes lower hsp response
Diem et al, 2005. Mutation Res	1800MHz	fibroblasts, GFSH-R-17 granulosa cells non-thermal DNA breakage
Fritze et al, 1997 Neuroscience	900MHz	rat brain blood brain barrier leakage at high SAR
Goodman et al, 1983 Science	pulsed 60Hz	*Sciara* larvae induce cellular transcription
Goodman et al, 1994 Bioelectrochem Bioenerg	60Hz	*Sciara* larvae increased hsp70 transcripts
Harvey et al, 2000 Cell Biol Int	864.3MHz	human mast cell line, HMC-1 effects on protein kinase C , stress genes
Hirose et al, 2006a Bioelectromagnetics	2.1425GHz	Human IMR-90 fibroblasts **NO** effect on gene expression of p53
Hirose et al, 2006b Bioelectromagnetics	2.1425GHz	human glioblastoma A172, IMR-90 fibroblasts **NO** effect on apoptosis, phosphorylation of hsp27
Ivancsits et al, 2005 Mutation Res	intermittent 50Hz	**NO** effect lymphocyte, monocyte, muscle: DNA damage: fibroblast, melanocyte, rat granulose
Jin et al, 1997 Bioelectrochem Bioenerg	60Hz	HL60 cells from two sources *myc* expression in one population, not in other
Kwee et al, 2001 Electro- and Magnetobiology	960MHz	human epithelial amnion (AMA) cells hsp70 increased

Table 1. Studies of EMF Stimulation of DNA and Protein Synthesis
(page 3)

Lacy-Hulbert et al, 1995 Radiation Res	50Hz	HL60 **NO** synthesis of myc or β-actin
Lai & Singh, 1997a Bioelectromagnetics	60Hz	rat brain cells melatonin blocks DNA strand breaks
Lai & Singh, 2005 Electromag Biol Med	1800MHz	rat brain cells noise blocks DNA strand breaks
Lantow et al, 2006a Radiation Res	1800MHz	human Mono Mac 6 and K562 cells **NO** hsp response
Lantow et al, 2006b Radiat Environ Biophys	1800MHz	primary human monocytes, lymphocytes **NO** hsp response
Lantow et al, 2006c Radiation Res	1800MHz	human Mono Mac 6 and K562 cells **NO** effect on apoptosis or necrosis
Laszlo et al, 2005 Radiation Res	835MHz	cultured mammalian cells **NO** 'effect within sensitivity of assay'
Laubitz et al, 2006 Experimental Physiol	muscle generated ELF	E coli, Caco-2 cells induce hsp70, protect vs apoptosis
Lee JS et al, 2005 Int J Radiat Biol	849, 1763 MHz	hsp70.1-deficient mice **NO** hsp induction
Lee S et al, 2005 FEBS Lett	2.45GHz	cultured human cells gene regulation: apoptosis 88, cell cycle99
Leszczynski et al, 2002 Differentiation	900MHz	human endothelial cells activate hsp27/p38MAPK stress pathway
Liburdy et al, 1993 J Pineal Res	60Hz	ER^+ MCF7 breast cancer cells block melatonin's oncostatic action
Lim et al, 2005 Radiation Res	900MHz	human leukocytes. **NO** effect on hsp
Lin et al, 1994 J Cell Biochem	60Hz	human HL60 cells EMF region of the c-*myc* promoter

Table 1. Studies of EMF Stimulation of DNA and Protein Synthesis (page 4)

Lin et al, 1996 Bioelectrochem Bioenerg	60Hz	human HL60 cells changes in c-myc transcript levels
Lin et al, 1999 J Cell Biochem	60Hz	human HL60 cells EMF consensus sequence in HSP70 promoter
Lin et al, 2001 J Cell Biochem	60Hz	human HL60 cells EMF consensus sequence response elements
Lixia et al, 2006 Mutat Res	1.8GHz	human lens epithelial cells increased hsp70 protein
Maes et al, 2006 [Epub] Mutagenesis	900MHz	peripheral blood lymphocytes **NO** effect on DNA damage
Malagoli et al, 2004 Comp Biochem Physiol	50Hz	mussel immunocyte activate p38 MAP kinase, induce hsp70, hsp90
Mashevich et al, 2003 Bioelectromagnetics	830MHz	human peripheral blood lymphocytes chromosomal instability
McNamee et al, 2002 Radiat Res	1.9Ghz	human leukocytes **NO** effect on DNA damage, micronuclei
Miyakawa et al, 2001 Bioelectromagnetics	60Hz	C elegans induction of hsp16
Nylund & Leszczynski,2004 Proteomics	900MHZ	human endothelial cell line EA.hy926 effects on cytoskeletal proteins
Nylund & Leszczynski,2006 Proteomics	900MHZ	human endothelial cell line EA.hy926 response genome- and proteome-dependent
Oktem et al, 2005. Arch Med Res	900MHz	rats (oxidative kidney damage) oxidative damage protected by melatonin
Ozguner et al, 2005 Toxicol Ind Health	900MHz	rats (oxidative myocardial damage) protection by caffeic acid phenethyl ester

Table 1. Studies of EMF Stimulation of DNA and Protein Synthesis (page 5)

Penafiel et al, 1997 Bioelectromagnetics	840MHz (AM, FM)	mouse L929 cells (ornithine decarboxylase activity) frequency dependent AM effect, no FM effect
Phillips et al, 1998 Bioelectrochem Bioenerg	813, 836MHz	Molt-4 T-lymphoblastoid cells DNA damage (and ability to repair) varied with SAR
Saffer & Thurston, 1995 Radiation Res	60Hz	HL60, Daudi cells **NO** synthesis of myc
Sanchez et al, 2006 FEBS J	900MHz	human skin cells slight but significant increase in hsp70
Sarimov et al, 2004 IEEE Trans Plasma Sci	895, 915MHz	transformed human lymphocytes affect chromatin conformation
Shallom et al, 2002 J Cell Biochem	915MHz	chick embryos induces hsp70, protects against hypoxia
Shi et al, 2003. Environ health Perspect	60Hz	human keratinocytes **NO** phosphorylation, expression of hsp27
Simko et al, 2006 Toxicol Lett	900MHz	human Mono Mac 6 cells **NO** hsp reponse
Vanderwaal et al, 2006 \Int J Hyperthermia	900MHz	cultured HeLa, S3 and EA Hy296 cells **NO** hsp27 phosphorylation increases
Velizarov et al, 1999 Bioelectrochem Bioenerg	960MHz	human epithelial cells cell proliferation
Wang et al, 2006 Bioelectromagnetics	2450MHz	human glioma A172 cells **NO** hsp70, hsp27
Weisbrot et al, 2003 J Cell Biochem	900MHz	*Drosophila* hsp708, affects development, reproduction
Winker et al, 2005 Mutation Res	intermittent 50Hz	human diploid fibroblasts micronuclei, chromosomal damage

Table 2 Biological Thresholds in the ELF Range

Biological System	Threshold*	Reference
Enzyme reaction rates		
Na,K-ATPase	.2-.3μT	Blank & Soo, 1996
cytochrome oxidase	.5-.6μT	Blank & Soo, 1998
ornithine decarboxylase	~2μT	Mullins et al, 1999
Oxidation-reduction rate		
Belousov-Zhabotinsky	<.5μT	Blank & Soo, 2001b
Biosynthesis of stress proteins		
HL60, Sciara, yeast,	<.8μT	Goodman et al, 1994
breast (HTB124, MCF7)	<.8μT	Lin et al, 1998
chick embryo (anoxia)	~2μT	DiCarlo et al, 2000
Disease related block melatonin inhibition		
of breast carcinoma	.2<1.2μT	Liburdy et al, 1993
leukemia epidemiology	.3-.4μT	Ahlbom et al, 2000
		Greenland et al, 2000

*The estimated values are for departures from the baseline, although Mullins et al (1999) and DiCarlo et al (2000) generally give inflection points in the dose-response curves. The leukemia epidemiology values are not experimental and are listed for comparison.

SECTION 8

EVIDENCE FOR EFFECTS ON THE IMMUNE SYSTEM

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Appendix 8-A Some legal aspects of the functional impairment electrohypersensitivity in Sweden

I. Basic concepts and components of the immune system

The human immune system is part of a general defense barrier towards our surrounding environment. We live in a biological system, the world, dominated by various microorganisms, including microbes and viruses, many of which can cause harm. The immune system serves as the primary line of defense against invasion by such microbes. As we are, practically speaking, built as a tube, the outer surface - the skin - and the innermost surface - the gastrointestinal tract - are the major borders between us and the rest of the universe. These borders must be guarded and protected since any damage to them could be fatal.

The skin and the mucous membranes are part of the innate or non-adaptive immune system. However, if these barriers are broken (e.g. after cutting a finger), then microbes, including potential pathogens (i.e. harmful microbes) can enter the body and then begin to multiply rapidly in the warm, moist, nutrient-rich environment. The cut may not be as physical, brutal and abrupt as a knife cut, it could also very well be an internal leakage, such as the one found after microwave exposure of the fragile blood-brain-barrier (cf. Persson et al, 1997). Such a leakage could indeed be fatal, causing nerve cell damage and consecutive cellular death (cf. Salford et al, 2003).

One of the first cell types to be encountered by a foreign organism after a cut in the skin is the phagocytic white blood cells which will congregate within minutes and begin to attack the invading foreign microbes. Following this, the next cell type to be found in the area of such a local infection will be the so-called neutrophils. They are also phagocytic and use pattern-regonizing surface receptor molecules to detect structures commonly found on the surface of bacteria. As a result, these bacteria - as well as other forms of particulate materia - will be ingested and degraded by the neutrophils. Various other protein components of serum, including the complement components may bind to the invader organisms and facilitate their phagocytosis, thereby further limiting the source of infection/disease. Other small molecules, the interferons, mediate an early response to viral infection by the innate system.

The innate immune system is often sufficient to destroy invading microbes. If it fails to clear an infection, it will rapidly activate the adaptive or acquired immune response, which - as a consequence - takes over.The molecular messenger connection between the innate and the adaptive systems are molecules known as cytokines (actually, the interferons are part of this molecular family).

The first cells in this cellular orchestra to be activated are the T and B lymphocytes. These cells are normally at rest and are only recruited at need, i.e. when encountering a foreign (=non-self) entity referred to as an antigen. The T and B lymphocytes, together with a wide spectrum of other cell types, have antigen receptors or antigen-recognizing molecules on their surface. Among them you find the classical antibodies (=B cell antigen receptors), T cell antigen receptors as well as the specific protein products of special genetic regions (=the major histocompatibility complexes). The genes of humans are referred to as human leukocyte antigen (HLA) genes and their protein products as HLA molecules. The antibodies - apart from being B cell surface receptors - are also found as soluble antigen-recognizing molecules in the blood

(immunoglobulins). The adaptive immune response is very highly effective but rather slow; it can take 7-10 days to mobilize completely. It has a very effective pathogen (non-self) recognition mechanism, a molecular memory and can improve it's production of pathogen-recognition molecules during the response.

A particularly interesting set of cells are the various dendritic cells of the skin. In the outermost portion, the epidermis, you find both dendritic melanocytes, the cells responsible for the pigment-production, as well as the Langerhans cells with their antigen-presenting capacity. In the deeper layer, the dermis, you find corresponding cells, as well as the basophilic mast cells, often showing a distinct dendritic appearance using proper markers such as chymase, tryptase or histamine. All these cells are the classical reactors to external radiation, such as radioactivity, X-rays and UV light. For that reason, our demonstration (Johansson et al, 1994) of a high-to-very high number of somatostatin-immunoreactive dendritic cells in the skin of persons with the functional impairment electrohypersensitivity is of the greatest importance. Also, the alterations found in the mast cell population of normal healthy volunteers exposed in front of ordinary house-hold TVs and computer screens (Johansson et al, 2001) are intriguing, as are the significantly increased number of serotonin-positive mast cells in the skin ($p<0.05$) and neuropeptide tyrosine (NPY)-containing nerve fibers in the thyroid ($p<0.01$) of rats exposed to extremely low-frequency electromagnetic fields (ELF-EMF) compared to controls, indicating a direct EMF effect on skin and thyroid vasculature (Rajkovic et al, 2005a,b, 2006; for further details and refs., see below). In the gastrointestinal tract, you will find corrsponding types of cells guardening our interior lining towards the universe.

In essence, the immune system is a very complex one, built up of a large number of cell types (B and T lymphocytes, macrophages, natural killer cells, mast cells, Langerhans cells, etc.) with certain basic defense strategies. It has evolved during an enormously long time-span and is constructed to deal with it's known enemies, including bacteria. Among the known enemies are, of course, not modern electromagnetic fields, such as power-frequent electric and magnetic fields, radiowaves, TV signals, mobile phone or Wi-Fi microwaves, radar signals, X-rays or radioactivity. They have been introduced during the last 100 years, in many cases during the very last decades. They are an entirely new form of exposure and could pose to be a biological "terrorist army" against which there are no working defence walls. They do penetrate the body from outside and in. Some of them have already been proven to be of fatal nature, and today no-one would consider having a radioactive wrist watch with glowing digits (as you could in the 1950s), having your children's shoes fitted in a strong X-ray machine (as you could in the 1940s), keeping radium in open trays on your desk (as scientists could in the 1930s), or X-raying each other at your garden party (as physicians did in the 1920s). That was, of course, just plain madness. However, the persons doing so and selling these gadgets were not misinformed or less intelligent, not at all. The knowledge at the time was just lacking as was a competent risk analysis behaviour coupled to a parallel analysis of true public need.

II. Hypersensitivity reactions

The immune system can react in an excessive manner and it can cause damage to the local tissue as well as generally to the entire body. Such events are called

hypersensitivity reactions and they occur in response to three different types of antigens: a) infectious agents, b) environmental disturbances, and c) self-antigens. The second one is related to the impact of the new electromagnetic fields of today's modern world. Hypersensitivity can occur in response to innocuous environmental antigens - one example of this is allergy. For example, in hay fever, grass pollens themselves are incapable of causing damage; it is the immune response to the pollen that causes harm.

II A. Hypersensitivity to environmental substances

For environmental substances to trigger hypersensitivity reactions, they must be fairly small in order to gain access to the immune system. Dust triggers off a range of responses because they are able to enter the lower extremities of the respiratory tract, an area that is rich in adaptive immune-response cells. These dusts can mimic parasites and may stimulate an antibody response. If the dominant antibody is IgE, they may subsequently trigger immediate hypersensitivity, which is manifest as allergies such as asthma or rhinitis, If the dust stimulates IgG antibodies it may trigger off a different kind of hypersensitivity, e.g. farmer's lung.

Smaller molecules sometimes diffuse into the skin and these may act as haptens, triggering a delayed hypersensitivity reaction. This is the basis of contact dermatitis caused by nickel.

Drugs administered orally, by injection or onto the surface of the body can elicit hypersensitivity reactions mediated by IgE or IgG antibodies or by T cells. Immunologically mediated hypersensitivity reactions to drugs are very common and even very tiny doses of drugs can trigger life-threatening reactions. These are well classified as idiosyncratic adverse drug reactions.

In this respect, of course electromagnetic fields could be said to fulfil the most important demands: they can penetrate the entire body and if they are small.

II B. Hypersensitivity to self antigens

Some degree of immune response to self antigens is normal and is present in most people. When these become exaggerated or when tolerance to further antigens breaks down, hypersensitivity reactions can occur and manifest themselves as an autoimmune disease, many of which that are truly serious and may even end fatally.

II C. Types of hypersensitivity reactions

The hypersensitivity classification system was first described by Coombs and Gell. The system classifies the different types of hypersensitivity reaction by the types of immune responses involved. Each type of hypersensitivity reaction produces characteristic clinical diseases whether the trigger is an enviromental, infectious or self-antigen. For example, in type III hypersensitivity the clinical result is similar whether the antigen is streptococcus, a drug or an autoantigen such as DNA.

Hypersensitivity reactions are reliant on the adaptive immune system. Prior exposure to antigen is required to prime the adaptive immune response to produce IgE (type I),

IgG (type II and III) or T cells (type IV). Because prior exposure is required, hypersensitivity reactions do not take place when an individual is first exposed to antigen. In each type of hypersensitivity reaction the damage is caused by different adaptive and innate systems, each of which with their respective role in clearing infections.

Type I
Type I hypersensitivity is mediated through the degranulation of mast cells and eosinophils. The effects are felt within minutes of exposure and this type of hypersensitivity is sometimes referred to as immediate hypersensitivity and is also known as allergy. Among such reactions are hay fever and the classical skin prick test that can be used to reveal such reaction patterns. -The mast cell is a common denominator in the functional impairment electrohypersensitivity (earlier referred to as "electrical allergy").

Type II
Type II hypersensitivity is caused by IgG reacting with antigen present on the surface of cells. The bound immunoglobulin then interacts with complement or with Fc receptors on macrophages. These innate mechanisms then damage the target cells using processes that may take several hours, as in the case of drug-induced hemolysis.

Type III
Immunoglobulin is also responsible for the type III hypersensitivity. In this case, immune complexes of antigen and antibody form and either cause damage at the site of production or circulate and cause damage elsewhere. Immune complexes take some time to form and to initiate tissue damage. Among the cells types involved are neutrophils. Post-streptococcal glomerulonephritis is a good example of immune complex disease.

Type IV
The slowest form of hypersensitivity is that mediated by T cells (type IV hypersensitivity). This can take 2-3 days to develop and is referred to as delayed hypersensitivity. Macrophages are frequently involved. A well-known example of such delayed reactions is contact dermatitis.

III. The old and new electromagnetic environment

"Electromagnetic radiation" covers a broad range of frequencies (over 20 orders of magnitude), from low frequencies in electricity supplies, radiowaves and microwaves, infrared and visible light, to x-rays and cosmic rays.

III A. Definitions and sources

Electric fields are created by differences in voltage: the higher the voltage, the stronger will be the resultant field. Magnetic fields are created when electric current flows: the greater the current, the stronger the magnetic field. An electric field will exist even when there is no current flowing. If current does flow, the strength of the magnetic field will vary with power consumption but the electric field strength will be constant.

III B. Natural sources of electromagnetic fields
Electromagnetic fields are present everywhere in our environment but are invisible to the human eye. Electric fields are produced by the local build-up of electric charges in the atmosphere associated with thunderstorms. The earth's magnetic field causes a compass needle to orient in a North-South direction and is used by birds and fish for navigation.

III C. Human-made sources of electromagnetic fields
Besides natural sources the electromagnetic spectrum also includes fields generated by human-made sources: X-rays are employed to diagnose a broken limb after a sport accident. The electricity that comes out of every power socket has associated low frequency electromagnetic fields. And various kinds of higher frequency radiowaves are used to transmit information – whether via TV antennas, radio stations or mobile phone base stations.

III D. What makes the various forms of electromagnetic fields so different?
One of the main characteristics which defines an electromagnetic field (EMF) is its frequency or its corresponding wavelength. Fields of different frequencies interact with the body in different ways. One can imagine electromagnetic waves as series of very regular waves that travel at an enormous speed, the speed of light. The frequency simply describes the number of oscillations or cycles per second, while the term wavelength describes the distance between one wave and the next. Hence wavelength and frequency are inseparably intertwined: the higher the frequency the shorter the wavelength.

III E. A few basic facts
Field strength: An electromagnetic field consist of an electrical part and a magnetic part. The electrical part is produced by a voltage gradient and is measured in volts/metre. The magnetic part is generated by any flow of current and is measured in Tesla. For example, standing under a power line would expose you to an electrical voltage gradient due to the difference between the voltage of the line (set by the power company) and earth. You would also be exposed to a *magnetic* field proportional to the current actually flowing through the line, which depends on consumer demand. Both types of field give biological effects, but the magnetic field may be more damaging since it penetrates living tissue more easily. Magnetic fields as low as around 2 milligauss (mG) or 0.2 microTesla (a millionth of a Tesla) can produce biological effects. For comparison, using a mobile (cell) phone or a PDA exposes you to magnetic pulses that peak at several tens of microTesla (Jokela et al, 2004; Sage et al, 2007), which is well over the minimum needed to give harmful effects. Because mobile phones and other wireless gadgets are held close to the body and are used frequently, these devices are potentially the most dangerous sources of electromagnetic radiation that the average person possesses.

Frequency: The fields must vary with time, e.g. those from alternating currents, if they are to have biological effects. Extremely low frequencies (ELF) represent power-lines and domestic appliances, and here, just now in June 2007, the WHO again has pointed them out as an area for general caution since they are believed to be one of the causes for children's leukemia. Pulsed or amplitude modulated, at a biologically active lower frequency (i.e. when the radio signal strength rises and falls in time with

the lower frequency), high-frequencies are the hallmark of mobile phones, WiFi systems, PDAs, etc.

III F. Electromagnetic fields at low frequencies

Electric fields exist whenever a positive or negative electrical charge is present. They exert forces on other charges within the field. The strength of the electric field is measured in volts per metre (V/m). Any electrical wire that is charged will produce an associated electric field. This field exists even when there is no current flowing. The higher the voltage, the stronger the electric field at a given distance from the wire. Electric fields are strongest close to a charge or charged conductor, and their strength rapidly diminishes with distance from it. Conductors such as metal shield them very effectively. Other materials, such as building materials and trees, provide some shielding capability. Therefore, the electric fields from power lines outside the house are reduced by walls, buildings, and trees. When power lines are buried in the ground, the electric fields at the surface are hardly detectable.

Plugging a wire into an outlet creates electric fields in the air surrounding the appliance. The higher the voltage the stronger the field produced. Since the voltage can exist even when no current is flowing, the appliance does not have to be turned on for an electric field to exist in the room surrounding it.

Magnetic fields arise from the motion of electric charges. The strength of the magnetic field is measured in amperes per meter (A/m); more commonly in electromagnetic field research, scientists specify a related quantity, the flux density (in microtesla, μT) instead. In contrast to electric fields, a magnetic field is only produced once a device is switched on and current flows. The higher the current, the greater the strength of the magnetic field.

Like electric fields, magnetic fields are strongest close to their origin and rapidly decrease at greater distances from the source. Magnetic fields are not blocked by common materials such as the walls of buildings.

III G. How do static fields differ from time-varying fields?

A static field does not vary over time. A direct current (DC) is an electric current flowing in one direction only. In any battery-powered appliance the current flows from the battery to the appliance and then back to the battery. It will create a static magnetic field. The earth's magnetic field is also a static field. So is the magnetic field around a bar magnet which can be visualized by observing the pattern that is formed when iron filings are sprinkled around it.

In contrast, time-varying electromagnetic fields are produced by alternating currents (AC). Alternating currents reverse their direction at regular intervals. In most European countries electricity changes direction with a frequency of 50 cycles per second or 50 Hertz. Equally, the associated electromagnetic field changes its orientation 50 times every second. North American electricity has a frequency of 60 Hertz.

What are the main sources of low, intermediate and high frequency fields? The time-varying electromagnetic fields produced by electrical appliances are an example of extremely low frequency (ELF) fields. ELF fields generally have frequencies up to

300 Hz. Other technologies produce intermediate frequency (IF) fields with frequencies from 300 Hz to 10 MHz and radiofrequency (RF) fields with frequencies of 10 MHz to 300 GHz. The effects of electromagnetic fields on the human body depend not only on their field level but on their frequency and energy. Our electricity power supply and all appliances using electricity are the main sources of ELF fields; computer screens, anti-theft devices and security systems are the main sources of IF fields; and radio, television, radar and cellular telephone antennas, and microwave ovens are the main sources of RF fields. These fields induce currents within the human body, which if sufficient can produce a range of effects such as heating and electrical shock, depending on their amplitude and frequency range. (However, to produce such effects, the fields outside the body would have to be very strong, far stronger than present in normal environments.)

There are four phenomena that emerge from the use of electricity: ground currents; "electromagnetic smog" from communications equipment; magnetic fields from power lines and specialized equipments; and radiofrequencies on power lines or so-called "dirty electricity." They may all be potential environmental toxins and this is an area of research that must be further pursued.

Electromagnetic fields at high frequencies

Mobile telephones, television and radio transmitters and radar produce RF fields. These fields are used to transmit information over long distances and form the basis of telecommunications as well as radio and television broadcasting all over the world. Microwaves are RF fields at high frequencies in the GHz range. In microwaves ovens, we use them to quickly heat food at 2.45 GHz (or 2,450 MHz).

Communications and radar antennae expose those who live or work near these installations to their emissions. The radiation travels through buildings, and can also be conducted along electrical wires or metal plumbing. Wireless communications create levels within buildings that are orders of magnitude higher than natural background levels.

At radio frequencies, electric and magnetic fields are closely interrelated and we typically measure their levels as power densities in watts per square metre (W/m^2).

IV. The immune system and the impairment electrohypersensitivity

An increasing number of studies has clearly shown various biological and medical effects at the cellular level of electromagnetic fields, including power-frequency and radiofrequency/microwave exposures at low-intensity levels. –Such electromagnetic fields are present in everyday life, at the workplace, in ~~your home~~ in homes and at places of leisure. Such bioeffects and health impacts are substantially documented in the scientific literature, and are directly relevant to public health.

Direct effects on the immune system were first reported in relation to people with symptoms of electrohypersensitivity. Subjective and objective skin- and mucosa-related symptoms, such as itch, smarting, pain, heat sensation, redness, papules,

pustles, etc., after exposure to visual display terminals (VDTs), mobile phones, DECT telephones, WI-FI equipments, as well as other electromagnetic devices were reported. Frequently, symptoms from internal organ systems, such as the heart and the central nervous system were reported.

A working definition of EHS from Bergqvist et al. (1997) is:

"a phenomenon where individuals experience adverse health effects while using or being in the vicinity of devices emanating electric, magnetic or electromagnetic fields (EMFs)".

Stenberg (2004) distinguishes between two groups: those who experience facial skin symptoms in connection with VDT work (sensory sensations of the facial skin including stinging, itching, burning, erythema, rosacea) while EHS symptoms include these and also fatigue, headache, sleeplessness, dizziness, cardiac and cognitive problems.

Hillert (2004) reports that symptoms of EHS may include facial skin complaints, eye irritation, runny or stuffy nose, impaired sense of smell, hoarse dry throat, coughing, sense of pressure in ear(s), fatigue, headache, heaviness in the head, nausea/dizziness, and difficulties in concentrating.

Cox (2004) reported on a study of electrical hypersensitivity in the United Kingdom. Symptoms reported by mobile phone users included headaches (85%), dizziness (27%), fatigue (24%), nausea (15%), itching (15%), redness (9%), burning 61%), and cognitive problems (42%). For those individuals reporting EHS symptoms in the UK population, the percentage of patients with symptoms from cell phone masts was 18%, DECT cordless phones (36%), landline phones (6%), VDTs (27%), television (12%) and fluorescent lights (18%).

Fox et al (2004) reported that a questionnaire survey of EHS individuals revealed symptoms of nausea, muzziness/disorientation.

Levallois et al. (2002) reported on their study of prevalence of self-perceived hypersensitivity to electromagnetic fields in California. They found that about 3% of the population reports to be electrohypersensitive. About 0.5% of the population has reported the necessity to change jobs or to remain unemployed due to the severity of their electrohypersensitivity symptoms. Underestimation of these percentages is discussed, since the population surveyed was found through contact with either an occupational clinic or a support group, and electrohypersensitive people very frequently cannot due normal outings (go out, travel, meet in buildings with EMF exposures, etc). The study concludes that while there was no clinical confirmation of the reported symptoms of electrohypersensitivity, the perception is of public health importance in California, and perhaps North America. The results were based on a telephone survey among a sample of 2,072 Californians. Being "allergic or very sensitive" to getting near electrical devices was reported by 68 subjects resulting in an adjusted prevalence of 3.2% (95% confidence interval: 2.8, 3.7). Twenty-seven subjects (1.3%) reported sensitivity to electrical devices but no sensitivity to chemicals. Alleging that a doctor had diagnosed "environmental illness or multiple chemical sensitivity" was the strongest predictor of reporting being hypersensitive to

EMF in this population (adjusted prevalence odds ratio = 5.8, 95 % confidence interval: 2.6 - 12.8. This study confirms the presence of this self-reported disorder in North America.

A recent German survey suggests that the prevalence of subjects who attribute health complaints to EMF exposures is not negligible. In a sample of 2,500 interviewees, 8% specifically attributed health complaints to exposures from mobile phone base station antennas or the use of mobile or cordless phones [Institut für angewandte Sozialwissenschaft (infas), 2004]. In Sweden, 3.1% of the population claimed to be hypersensitive to EMF. Considerable variation across countries, regions within countries, and surveys in the same regions has been noted before. In 1997, a European expert group reported that electrical hypersensitivity had a higher prevalence in Sweden, Germany, and Denmark than in the United Kingdom, Austria, and France [European group of experts, 1997]. All these data suggest that the true number is still uncertain and the topic merits further research (cf. Schuz et al, 2006).

Roosli et al. (2004a, 2004b) estimates that the proportion of individuals in Switzerland with EHS symptoms is about 5%, where the exposures of concern are cited to be powerlines, handheld phones, television and computer exposures rather than base stations (cell towers). He reported that about half the Swiss population is concerned about health effects from EMF exposures in general.

V. Scientific studies of electrohypersensitivity, as well as effects of electromagnetic fields on humans

Lyskov et al. (2004) reported that EHS individuals exhibited sensitivity to VDTs, fluorescent lights and television, all of which produce flickering light. EHS individuals that were given provocation tests with flickering light exhibited a higher critical flicker frequency (CFF) than normal, and their visual evoked potential (VEP) was significantly higher than in controls. Follow-up studies, individuals with EHS demonstrated increased CFF, increased VEP, increased heart rate, decreased heart rate variability (HRV) and increased electrodermal (EDA) reaction to sound stimuli. These results indicate an imbalance in the autonomic nervous system and a lack of normal circadian rhythms in these EHS individuals. However, it may also just show that they feel ill.

Mueller and Schierz (2004) reported that soundness of sleep and well-being in the morning but not sleep quality were affected by exposure in EHS individuals to overnight EMF exposures. An effect was reported where EHS individuals shifted their position in the bed during sleep to the non-exposed (or probably less exposed) side of the bed.

Vecchio et al (2007) have reported that EMF from mobile phones affects the synchronization of cerebral rhythms. Their findings suggest that prolonged exposure to mobile phone emissions affect cortical activity and the speed of neural synchronization by interhemispherical functional coupling of EEG rhythms. This may be evidence that such exposure can affect the way in which the brain is able to process information, by interfering with the synchronization rhythms between the

halves of the brain, and by disregulating the normal alpha wave 2 (about 8-10 Hz) and alpha 3 (10-12 Hz) bands.

Markova et al. (2005) reported that non-thermal microwave exposure from Global System for Mobile Communication (GSM) mobile telephones at lower levels than the ICNIRP safety standards affect 53BP1 and γ-H2AX foci and chromatin conformation in human lymphocytes. They investigated effects of microwave radiation of GSM at different carrier frequencies on human lymphocytes from healthy persons and from persons reporting hypersensitivity to electromagnetic fields (EMFs). They measured the changes in chromatin conformation, which are indicative of stress response and genotoxic effects, by the method of anomalous viscosity time dependence, and analyzed tumor suppressor p53-binding protein 1 (53BP1) and phosphorylated histone H2AX (γ-H2AX), which have been shown to colocalize in distinct foci with DNA double-strand breaks (DSBs), using immunofluorescence confocal laser microscopy. The authors reported that microwave exposure from GSM mobile telephones affect chromatin conformation and 53BP1/γ-H2AX foci similar to heat shock. For the first time, they reported that effects of microwave radiation from mobile telephones on human lymphocytes are dependent on carrier frequency. On average, the same response was observed in lymphocytes from hypersensitive and healthy subjects. These effects occurred at non-thermal microwave exposure levels from mobile telephones. These levels are presently permissible under safety standards of the International Commission for Non-Ionizing Radiation Protection (ICNIRP).

Recent evidence has indicated activation of stress-induced pathways in cultivated cells in response to microwaves (Leszczynski et al, 2002). Their article indicated that mobile telephone microwaves activate a variety of cellular signal transduction pathways, among them the hsp27/p38MAPK stress response pathway (Leszczynski et al, 2002). Whether activation of stress response pathways relates to apoptosis, blood-brain barrier permeability, or increased cancer in humans remains to be investigated. Further work reported gene and protein expression changes in human endothelial cell lines with microwave 900 MHz mobile phone exposure (Leszczynski and Nylund, 2006).

Persons claiming adverse skin reactions after having been exposed to computer screens or mobile phones very well could be reacting in a highly specific way and with a completely correct avoidance reaction, especially if the provocative agent was radiation and/or chemical emissions -- just as would happen if you had been exposed to e.g. sun rays, X-rays, radioactivity or chemical odors. The working hypothesis, thus, early became that they react in a cellularly correct way to the electromagnetic radiation, maybe in concert with chemical emissions such as plastic components, flame retardants, etc., something later focussed upon by professor Denis L. Henshaw and his collaborators at the Bristol University (cf. Fews et al, 1999a,b). This is also covered in great depth by the author Gunni Nordström in her latest book (2004).

Very early immune cell alterations were observed when exposing two EHS individuals to a TV monitor (Johansson et al, 1994). In this people were placed in front of, in front of an ordinary TV set (an open provocation study). Subjects who regarded themselves as suffering from skin problems due to work at video display terminals were tested. Employing immunohistochemistry, in combination with a wide range of antisera directed towards cellular and neurochemical markers, we observed

and reported a high-to-very high number of somatostatin-immunoreactive dendritic cells as well as histamine-positive mast cells in skin biopsies from the anterior neck taken before the start of the provocation. At the end of the provocation the high number of mast cells was unchanged, however, all the somatostatin-positive cells had seemingly disappeared. The reason for this latter finding may be discussed in terms of loss of immunoreactivity, increase of breakdown, etc. The high number of mast cells present may explain the clinical symptoms of itch, pain, edema and erythema.

In facial skin samples of electrohypersensitive persons, the most common finding is a profound increase of mast cells as monitored by various mast cell markers, such as histamine, chymase and tryptase (Johansson and Liu, 1995). From these studies, it is clear that the number of mast cells in the upper dermis is increased in the electrohypersensitivity group. A different pattern of mast cell distribution also occurred in the electrohypersensitivity group, namely, the normally empty zone between the dermo-epidermal junction and mid-to-upper dermis disappeared in the electrohypersensitivity group and, instead, this zone had a high density of mast cell infiltration. These cells also seemed to have a tendency to migrate towards the epidermis (=epidermiotrophism) and many of them emptied their granular content (=degranulation) in the dermal papillary layer. Furthermore, more degranulated mast cells could be seen in the dermal reticular layer in the electrohypersensitivity group, especially in those cases which had the mast cell epidermiotrophism phenomenon described above. Finally, in the electrohypersensitivity group, the cytoplasmic granules were more densely distributed and more strongly stained than in the control group, and, generally, the size of the infiltrating mast cells was found to be larger in the electrohypersensitivity group as well. It should be noted, that increases of similar nature later on were demonstrated in an experimental situation employing normal healthy volunteers in front of visual display units, including ordinary house-hold television sets (cf. Johansson et al, 2001).

Mast cells, when activated, release a spectrum of mediators, among them histamine, which is involved in a variety of biological effects with clinical relevance, e.g., allergic hypersensitivity, itch, edema, local erythema, and many types of dermatoses. From the results of the above studies, it is clear that electromagnetic fields affect the mast cell, and also the dendritic cell, population, and may degranulate these cells.

The release of inflammatory substances, such as histamine, from mast cells in the skin results in a local erythema, edema, and sensation of itch and pain, and the release of somatostatin from the dendritic cells may give rise to subjective sensations of ongoing inflammation and sensitivity to ordinary light. These are, as mentioned, the common symptoms reported from persons suffering from electrohypersensitivity/screen dermatitis. Mast cells occur in the brain (Zhuang et al, 1999) and their presence may, under the influence of electromagnetic field and/or radiofrequency radiation exposure lead to chronic inflammatory response by the mast cell degranulation.

Mast cells are also present in the heart tissue and their localization is of particular relevance to their function. Data from studies made on interactions of electromagnetic fields with the cardiac function have demonstrated that changes are present in the heart after exposure to electromagnetic fields. Some electrically sensitive people have symptoms similar to heart attacks after exposure to electromagnetic fields.

We have also compared facial skin from electrohypersensitive persons with corresponding material from normal healthy volunteers (Johansson et al, 1996). The aim of the study was to evaluate possible markers to be used for future double-blind or blind provocation investigations. Differences were found for the biological markers calcitonin gene-related peptide (CGRP), somatostatin (SOM), vasoactive intestinal polypeptide (VIP), peptide histidine isoleucine amide (PHI), neuropeptide tyrosine (NPY), protein S-100 (S-100), neuron-specific enolase (NSE), protein gene product (PGP) 9.5 and phenylethanolamine N-methyltransferase (PNMT). The overall impression in the blind-coded material was such that it turned out easy to blindly separate the two groups from each other. However, no single marker was 100% able to pin-point the difference, although some were quite powerful in doing so (CGRP, SOM, S-100). In our on-going investigations, we have also found alterations of the Merkel cell number in the facial skin of electrohypersensitive persons (Yoshimura et al, 2006). However, it has to be pointed out that we cannot, based upon those results, draw any definitive conclusions about the cause of the changes observed. Blind or double-blind provocations in a controlled environment (Johansson et al, 2001) are necessary to elucidate the underlying causes for the changes reported in this particular investigation.

Gangi and Johansson (1997, 2000) have proposed models for how mast cells and substances secreted from them (e.g., histamine, heparin, and serotonin) could explain sensitivity to electromagnetic fields similar to those used to explain UV- and ionizing irradiation-related damages. We discuss an increasing number of persons who report cutaneous problems as well as symptoms from certain internal organs, such as the central nervous system and the heart, when being close to electric equipment. Many of these respondents are users of video display terminals, and have both subjective and objective skin- and mucosa-related symptoms, such as pain, itch, heat sensation, erythema, papules, and pustules. The central nervous system-derived symptoms are, e.g., dizziness, tiredness, and headache, erythema, itch, heat sensation, edema, and pain which are also common symptoms of sunburn (UV dermatitis). Alterations have been observed in cell populations of the skin of electrohypersensitive persons similar to those observed in the skin damaged due to ultraviolet light or ionizing radiation.

Gangi and Johansson (1997, 2000), have proposed a theoretical mechanism to explain how mast cells and substances secreted from them could cause sensitivity to electromagnetic fields. The mechanism derives from known facts in the fields of UV- and ionizing irradiation-related damage. Alterations seen after power-frequency or microwave electromagnetic field-exposures that result in electrohypersensitivity symptoms may be understood by comparison to to ionizing radiation damage according to the type of immune function responses seen in both.

The working hypothesis is that electrohypersensitivity is a kind of irradiation damage, since the observed cellular changes are very much the same as the ones documented in tissue subjected to UV-light or ionizing radiation (see references below).

Mast cells are located in close proximity to neurons in the peripheral and central nervous systems, suggesting a functional role in normal and aberrant neurodegenerative states. They also possess many of the features of neurons, in terms of monoaminergic systems, responsiveness to neurotrophins and neuropeptides and the ability to synthesise and release bioactive neurotrophic factors. Mast cells are able

to secrete an array of potent mediators which may orchestrate neuroinflammation and affect the integrity of the blood-brain barrier. The «cross-talk» between mast cells, lymphocytes, neurons and glia constitutes a neuroimmune axis which is implicated in a range of neurodegenerative diseases with an inflammatory and/or autoimmune component, such as multiple sclerosis and Alzheimer's disease.

Mast cells are involved in numerous activities ranging from control of the vasculature, to tissue injury and repair, allergic inflammation and host defences. They synthesize and secrete a variety of mediators, activating and modulating the functions of nearby cells and initiating complex physiological changes. Interestingly, NO produced by mast cells and/or other cells in the microenvironment appears to regulate these diverse roles. Some of the pathways central to the production of NO by mast cells and many of the tightly controlled regulatory mechanisms involved have been identified. Several cofactors and regulatory elements are involved in NO production, and these act at transcriptional and post-translational sites. Their involvement in NO production and the possibility that these pathways are critically important in mast cell functions should be investigated. The effects of NO on mast cell functions such as adhesion, activation and mediator secretion ought to be examined with a focus on molecular mechanisms by which NO modifies intracellular signalling pathways dependent or independent of cGMP and soluble guanylate cyclase. Metabolic products of NO including peroxynitrite and other reactive species may be the critical elements that affect the actions of NO on mast cell functions. Further understanding of the actions of NO on mast cell activities may uncover novel strategies to modulate inflammatory conditions.

It is important to remember that mastocytosis - an abnormal accumulation of mast cells in one or more organ system - can occur secondarily to other causes, such as inflammation and some kinds of leukemia. The increase in EHS being described here is more accurately thought of as "primary" mastocytosis, meaning that the increased number of mast cells occurs independently of any other cause. However, because of the increased number of mast cells in primary mastocytosis, conditions such as osteoporosis and inflammation may arise as a result of the activity of those mast cells. The manner in which primary mastocytosis can be distinguished from secondary mastocytosis and other conditions should be addressed.

Research of mast cells and mastocytosis has made impressive progress over the past decade toward understanding what is different about mast cells in patients who have mastocytosis compared with mast cells in people who do not. A group of 23 researchers from Europe and the United States met in Vienna in September, 2000, and, after lengthy discussions, arrived at a consensus as to what criteria will accurately diagnose mastocytosis, and how to classify the various sub-types. Their conclusions are reported in a series of articles in the July, 2001, issue of Leukemia Research. Unfortunately, nothing was mentioned about mast cells and EMF effects.

Patients with mastocytosis may or may not have constitutional symptoms, including weight loss, pain, nausea, headache, malaise, or fatigue. These symptoms may be due to uncontrolled proliferation of mast cells or involvement of distinct organs, such as the stomach and intestines, or bone or bone marrow. Constitutional symptoms also can result from high levels of mast cell mediators in the blood stream. The severity of symptoms varies from mild to life-threatening.

The study of biopsy tissue in patients with suspected mastocytosis requires the use of appropriate stains. Tryptase is the stain of choice, as toluidine blue and Giemsa stains are more likely to be affected by tissue processing and may not always produce reliable results.

In skin, accumulation of groups of mast cells combined with the presence of urticaria pigmentosa or mastocytoma is diagnostic of cutaneous mastocytosis. In some cases, it may be difficult to establish a diagnosis. The absence of skin lesions does not rule out the diagnosis of mastocytosis.

The abnormalities that may be seen in mastocytosis mast cells are elongated shape, oval nuclei that are not in the center of the mast cell, and fewer than usual granules inside the mast cells, with those present being in groups rather than scattered. If two or more of these features are found, the cells are referred to as atypical mast cells. Sometimes the nucleus of atypical mast cells will have "lobes."

When the diagnosis of mastocytosis has not previously been established, specialized analyses may be required to differentiate between mastocytosis and other non-mast cell disorders of the blood-forming system, such as leukemias and myeloproliferative disorders. In some of these other disorders, the diseased cells contain and release low amounts of tryptase. Additional blood cell studies and chromosome analysis may be necessary to make a clear diagnosis in such cases.

Holmboe and Johansson (2005) reported on testing for the presence of increased levels of IgE or signs of a positive Phadiatop Combi (which is a screening test for allergies towards certain articles of food, pollen, insects, and other animals) which both would be indicators of an immune system alert. Twenty-two people (5 men, 17 women) participated in the study. Skin and nervous system effects were the primary symptoms reported by participants in the study. The most frequently reported symptoms were skin redness, eczema and sweating, loss of memory, concentration difficulties, sleep disturbances, dizziness, muscular and joint-related pain, and muscular and joint-related weakness. Headache, faintness, nasal stuffiness, and fatigue were also common. In addition, 19 of the people had disturbances of the gastrointestinal tract. All the people with the impairment electrohypersensitivity had tinnitus.

No connection between IgE blood levels and symptoms were found. All the people who reported electrohypersensitivity had normal values (<122 kU/l). Only 3 people had a positive Phadiatop Combi. Such increases could be used in the diagnosis of electrohypersensitivity, but they were not found to be useful indicators.

Animal Studies

In addition to the studies in humans, series of animal experiments were performed in collaboration with the Department of Biology, Faculty of Sciences, Novi Sad, Serbia and Montenegro), and the Karolinska Institute, Stockholm, Sweden (Rajkovic et al, 2005a,b, 2006).

The aim of these was to investigate the influence of extremely low-frequency electromagnetic fields (ELF-EMFs) on mast cells, parafollicular cells, and nerve fibers in rat skin and thyroid gland, as seen using light and transmission electron

microscopy. The experiments were performed on 2-month-old Wistar male rats exposed for 4 h a day, 5 or 7 days a week for 1 month to power-frequent (50 Hz) EMFs (100-300 μT, 54-160 V/m). After sacrifice, samples of skin and thyroid were processed for indirect immunohistochemistry or toluidine blue staining and were then analyzed using the methods of stereology. Antibody markers to serotonin, substance P, calcitonin gene-related peptide (CGRP), and protein gene product 9.5 (PGP) were applied to skin sections and PGP, CGRP, and neuropeptide Y (NPY) markers to the thyroid. A significantly increased number of serotonin-positive mast cells in the skin ($p<0.05$) and NPY-containing nerve fibers in the thyroid ($p<0.01$) of rats exposed to ELF-EMF was found compared to controls, indicating a direct EMF effect on skin and thyroid vasculature.

After ultrastructural examination, a predominance of microfollicles with less colloid content and dilated blood capillaries was found in the EMF group. Stereological counting showed a statistically significant increase of the volume density of follicular epithelium, interfollicular tissue and blood capillaries as well as the thyroid activation index, as compared to the controls. The volume density of colloid significantly decreased. Ultrastructural analysis of thyroid follicular cells in the EMF group revealed the frequent finding of several colloid droplets within the same thyrocyte with the occasional presence of large-diameter droplets. Alterations in lysosomes, granular endoplasmic reticulum and cell nuclei compared to the control group were also observed. Taken together, the results of this study show the stimulative effect of power-frequency EMFs on thyroid gland at both the light microscope and the ultrastructural level.

The-animal results reported in these studies can not be explained away as psychosomatic in origin because they were conducted on animals, not humans.

In summary, both human and animal studies report large immunohistological changes in mast cells, and other measures of immune disfunction and disregulation due to exposures to ELF and RF at environmental levels associated with new electrical and wireless technologies.

It iss evident from our preliminary experimental data that various biological alterations are present in the electrohypersensitive persons claiming to suffer from exposure to electromagnetic fields. The alterations are themselves enough to fully explain the EHS symptoms, and the involvement of the immune system is evident. In view of recent epidemiological studies, pointing to a correlation between long-term exposure from power-frequent magnetic fields or microwaves and cancer, our data ought to be taken seriously and to be further analyzed.

Thus, it is of paramount importance to continue the investigation of persons with the impairment electrohypersensitivity. We would favour studies of electromagnetic fields' interaction with mast cell release of histamine and other biologically active substances, studies of lymphocyte viability as well as studies of the newly described serotonin-containing melanocytes. Also, continued analysis of the intraepidermal nerve fibers and their relations to these mast cells and serotonin-containing melanocytes are very important. Finally, not to be forgotten, a general investigation - of persons with the impairment electrohypersensitivity versus normal healthy volunteers - regarding the above markers as well as other markers for cell traffic,

proliferation and inflammation is very much needed. Such scientific work may lay a firm foundation for necessary adjustment of accessibility, thus helping and supporting all persons with the functional impairment electrohypersensitivity.

VI. Direct effects of EMFs on the immune system

Childhood leukemia was early connected to power-frequent magnetic fields already in the pioneering work by Wertheimer and Leeper (1979), and more recently Scandinavian scientists have identified an increased risk for acoustic neuroma (i.e., a benign tumor of the eighth cranial nerve) in cell phone users, as well as a slightly increased risk of malignant brain tumors such as astrocytoma and meningioma on the same side of the brain as the cell phone was habitually held (Hardell et al, 1999, 2004, 2005; Lonn et al, 2004). In addition, a clear association between adult cancers and FM radio broadcasting radiation has been noticed, both in time and location (Hallberg and Johansson, 2002b, 2004a, 2005a). Initial studies on facial nevi indicates that nowadays also young children can have a substantial amount of these. If it can be shown that radiofrequency radiation is not correlated with childhood cancers the current focus on low-frequency electromagnetic fields can continue. If there is also a radiofrequency and/or microwave correlation then this must be considered in future research as well as in today's preventive work.

Anane and coworkers (2003) studied the effects of acute exposure to GSM-900 microwaves (900 MHz, 217 Hz pulse modulation) on the clinical parameters of the acute experimental allergic encephalomyelitis (EAE) model in rats in two independent experiments: rats were either habituated or nonhabituated to the exposure restrainers. EAE was induced with a mixture of myelin basic protein and Mycobacterium tuberculosis. Female Lewis rats were divided into cage control, sham exposed, and two groups exposed either at 1.5 or 6.0 W/kg local specific absorption rate (SAR averaged over the brain) using a loop antenna placed over their heads. No effect of a 21-day exposure (2 h/day) on the onset, duration, and termination of the EAE crisis was seen.

The object of the study by Boscol et al. (2001) was to investigate the immune system of 19 women with a mean age of 35 years, for at least 2 years (mean = 13 years) exposed to electromagnetic fields induced by radiotelevision broadcasting stations in their residential area. In September 1999, the EMFs (with range 500 KHz-3 GHz) in the balconies of the homes of the women were (mean +/- S.D.) 4.3 +/- 1.4 V/m. Forty-seven women of similar age, smoking habits and atopy composed the control group, with a nearby resident EMF exposure of < 1.8 V/m. Blood lead and urinary trans-trans muconic acid (a metabolite of benzene), markers of exposure to urban traffic, were higher in the control women. The EMF exposed group showed a statistically significant reduction of blood NK CD16+-CD56+, cytotoxic CD3(-)-CD8+, B and NK activated CD3(-)-HLA-DR+ and CD3(-)-CD25+ lymphocytes. 'In vitro' production of IL-2 and interferon-gamma (INF-gamma) by peripheral blood mononuclear cells (PBMC) of the EMF exposed group, incubated either with or without phytohaemoagglutinin (PHA), was significantly lower; the 'in vitro' production of IL-2 was significantly correlated with blood CD16+-CD56+ lymphocytes. The stimulation index (S.I.) of blastogenesis (ratio between cell proliferation with and without PHA) of PBMC of EMF exposed women was lower than that of the control subjects. The S.I. of blastogenesis of the EMF exposed group

(but not blood NK lymphocytes and the 'in vitro' production of IL-2 and INF-gamma by PBMC) was significantly correlated with the EMF levels. Blood lead and urinary trans-trans muconic acid were barely correlated with immune parameters: the urinary metabolite of benzene of the control group was only correlated with CD16+-CD56+ cells indicating a slight effect of traffic on the immune system. In conclusion, this study demonstrates that high-frequency EMFs reduce cytotoxic activity in the peripheral blood of women without a dose-response effect. Such an effect could, of course, only be considered as very serious, since this could hamper the immune system in it's daily struggle against various organisms/agents.

On the other hand, Chagnaud and Veyret in 1999 could not demonstrate an effect of low-level pulsed microwaves on the integrity of the immune system. They investigated the effects of GSM-modulated microwaves on lymphocyte sub-populations of Sprague-Dawley rats and their normal mitogenic responses using flow cytometry analysis and a colorimetric method. No alterations were found in the surface phenotype of splenic lymphocytes or in their mitogenic activity.

Cleary et al. (1990) reported a biphasic, dose-dependent effect of microwave radiation on lymphycyte proliferation with non-thermal exposures. -Whole human blood was exposed or sham-exposed in vitro for 2 h to 27 or 2,450 MHz radio-frequency electromagnetic (RF) radiation under isothermal conditions (i.e., 37 +/- 0.2 degrees C). Immediately after exposure, mononuclear cells were separated from blood by Ficoll density-gradient centrifugation and cultured for 3 days at 37 degrees C with or without mitogenic stimulation by phytohemagglutinin (PHA). Lymphocyte proliferation was assayed at the end of the culture period by 6 h of pulse-labeling with 3H-thymidine (3H-TdR). Exposure to radiation at either frequency at specific absorption rates (SARs) below 50 W/kg resulted in a dose-dependent, statistically significant increase of 3H-TdR uptake in PHA-activated or unstimulated lymphocytes. Exposure at 50 W/kg or higher suppressed 3H-TdR uptake relative to that of sham-exposed cells. There were no detectable effects of RF radiation on lymphocyte morphology or viability. Notwithstanding the characteristic temperature dependence of lymphocyte activation in vitro, the isothermal exposure conditions of this study warrant the conclusion that the biphasic, dose-dependent effects of the radiation on lymphocyte proliferation were not dependent on heating.

Cleary et al. (1996) subsequently published ~~yet~~ another paper reporting a biphasic response of lymphycytes to radiofrequency/microwave radiation where higher SARs resulted in decreased cell proliferation and lower SARs result in increased cell proliferation, dependent on the mitotic state of the cells. -Previous in vitro studies had provided evidence that RF electromagnetic radiation modulates proliferation of human glioma, lymphocytes, and other cell types. The mechanism of such RF radiation cell proliferation modulation, as well as mechanisms for effects on other cell physiologic endpoints, however, were not well understood. To obtain insight regarding interaction mechanisms, they investigated effects of RF radiation exposure on interleukin 2 (IL-2) -dependent proliferation of cytolytic T lymphocytes (CTLL-2). After exposure to RF radiation in the presence or absence of IL-2 cells were cultured at various physiological concentrations of IL-2. Treatment effects on CTLL-2 proliferation were determined by tritiated thymidine incorporation immediately or 24 h after exposure. Exposure to 2,450 MHz RF radiation at specific absorption rates (SARs) of greater than 25 W/kg (induced E-field strength 98.4 V/m) induced a

consistent, statistically significant reduction in CTLL-2 proliferation, especially at low IL-2 concentrations. At lower SARs, 2,450 MHz exposure increased CTLL-2 proliferation immediately after exposure but reduced 24 h post-exposure proliferation. RF radiation effects depended on the mitotic state of the cells at the time of exposure.

In 1992, Czerska et al. studied the effects of continuous and pulsed 2,450-MHz radiation on spontaneous lymphoblastoid transformation of human lymphocytes in vitro. Normal human lymphocytes were isolated from the peripheral blood of healthy donors. One-ml samples containing one million cells in chromosome medium 1A were exposed for 5 days to conventional heating or to continuous wave (CW) or pulsed wave (PW) 2,450-MHz radiation at non-heating (37 degrees C) and various heating levels (temperature increases of 0.5, 1.0, 1.5, and 2 degrees C). The pulsed exposures involved 1-microsecond pulses at pulse repetition frequencies from 100 to 1,000 pulses per second at the same average SAR levels as the CW exposures. Actual average SARs ranged to 12.3 W/kg. Following termination of the incubation period, spontaneous lymphoblastoid transformation was determined with an image analysis system. The results were compared among each of the experimental conditions and with sham-exposed cultures. At non-heating levels, CW exposure did not affect transformation. At heating levels both conventional and CW heating enhanced transformation to the same extent and correlate with the increases in incubation temperature. PW exposure enhanced transformation at non-heating levels. This finding is significant ($p<0.002$). At heating levels PW exposure enhanced transformation to a greater extent than did conventional or CW heating. This finding is significant at the 0.02 level. It was concluded that PW 2,450-MHz radiation acts differently on the process of lymphoblastoid transformation in vitro compared with CW 2,450-MHz radiation at the same average SARs.

In 2003, Dabrowski et al. exposed samples of mononuclear cells isolated from peripheral blood of healthy donors ($n = 16$) to 1,300 MHz pulse-modulated microwaves at 330 pps with 5 μs pulse width. The samples were exposed in an anechoic chamber at the average value of power density of $S = 10$ W/m^2 (1 mW/cm^2). The average specific absorption rate (SAR) was measured in rectangular waveguide and the value of SAR = 0.18 W/kg was recorded. Subsequently, the exposed and control cells were assessed in the microculture system for several parameters characterizing their proliferative and immunoregulatory properties. Although the irradiation decreased the spontaneous incorporation of 3H-thymidine, the proliferative response of lymphocytes to phytohemagglutinin (PHA) and to Con A as well as the T-cell suppressive activity (SAT index) and the saturation of IL-2 receptors did not change. Nevertheless, the lymphocyte production of interleukin (IL)-10 increased ($p< 0.001$) and the concentration of IFNγ remained unchanged or slightly decreased in the culture supernatants. Concomitantly, the microwave irradiation modulated the monokine production by monocytes. The production of IL-1β increased significantly ($p< 0.01$), the concentration of its antagonist (IL-1ra) dropped by half ($p< 0.01$) and the tumor necrosis factor (TNF-α) concentration remained unchanged. These changes of monokine proportion (IL-1 β vs. IL-1ra) resulted in significant increase of the value of LM index ($p<0.01$), which reflects the activation of monocyte immunogenic function. The results indicate that pulse-modulated microwaves represent the potential of immunotropic influence, stimulating preferentially the immunogenic and proinflammatory activity of monocytes at relatively low levels of exposure,

Following these findings of G_o phase peripheral blood mononulclear cells (PBMC) exposed to low-level (SAR = 0.18 W/kg) pulse-modulated 1300 MHz microwave,s and subsequently cultured, demonstrating changed immune activity (as of above), in 2006 Stankiewicz and coworkers investigated whether cultured immune cells induced into the active phases of cell cycle (G_1, S) and then exposed to microwaves will also be sensitive to electromagnetic fields. An anechoic chamber containing a microplate with cultured cells and an antenna emitting microwaves (900 MHz simulated GSM signal, 27 V/m, SAR 0.024 W/kg) was placed inside an ASSAB incubator. The microcultures of PBMC exposed to microwaves demonstrated significantly higher response to mitogens and higher immunogenic activity of monocytes (LM index) than control cultures. The LM index, described in detail elsewhere (Dabrowski et al, 2001), represents the monokine influence on lymphocyte mitogenic response. The results suggest that immune activity of responding lymphocytes and monocytes can be additionally intensified by 900 MHz microwaves. The above described effects of an immune system activity-intensifying effect of 900 MHz microwaves are, of course, a very important warning signal as well as a very important piece of the explanatory jigsaw puzzle regarding, for instance, the functional impairment electrohypersensitivity. In the latter, affected persons very often describe "influenza-like" sensations in their body. Maybe the mobile phones, as well as other high-frequency devices, have aroused the immune system to a too high an activation level?

In an attempt to understand how non-atopic and atopic fertile women with uniform exposure to toxic compounds produced by traffic - immunologically react to high or low frequency electromagnetic fields (ELMF), Del Signore et al. (2000) performed a preliminary study. Women were divided in group A (non-atopic, non-exposed to ELMF); B (atopic, non-exposed to ELMF); C (non-atopic, exposed to ELMF); D (atopic, exposed to ELMF). In vitro cell proliferation of peripheral blood mononuclear cells (PBMC) of atopic women (groups B and D) stimulated by phytohaemoglutinin (PHA) was reduced. The ELMF exposed women (groups C and D) showed lower levels of blood NK CD16(+)-CD56+ lymphocyte subpopulations and of "in vitro" production of interferon-gamma (both spontaneously and in presence of PHA) by PBMC, suggesting that ELMF reduces blood cytotoxic activity. Serum IgE of the atopic women exposed to ELMF (group D) was higher than that of the other groups. Linear discriminant analysis including serum zinc and copper (essential enzymes for immune functions), blood lead and urinary transtrans muconic acid, a metabolite of benzene (markers of exposure to traffic) and key parameters of immune functions (CD16(+)-CD56+ lymphocyte subset, serum IgE, interferon-gamma produced by PBMC in presence of PHA, stimulation index of blastogenesis) showed absence of significant difference between groups A and C and a marked separation of groups B and D. This datum suggests that ELMF have a greater influence on atopic women exposed to traffic than on non-atopic ones, again pointing out differing reaction capacities in the human population – maybe dependent on varying immune functions based on variations in genetic make-up.

A more general reaction pattern was found by Dmoch and Moszczynski (1998) who assessed immunoglobulin concentrations and T-lymphocyte subsets in workers of TV re-transmission and satellite communication centres. An increase in IgG and IgA

concentrations, an increased count of lymphocytes and T8 lymphocytes, an decreased count of NK cells and a lower value of T-helper/T-suppressor ratio were found.

Elekes et al. (1996) found a very interesting sex-difference. The effect of continuous (CW; 2.45 GHz carrier frequency) or amplitude-modulated (AM; 50 Hz square wave) microwave radiation on the immune response was tested. CW exposures (6 days, 3 h/day) induced elevations of the number of antibody-producing cells in the spleen of male Balb/c mice (+37%). AM microwave exposure induced elevation of the spleen index (+15%) and antibody-producing cell number (+55%) in the spleen of male mice. No changes were observed in female mice. It is concluded that both types of exposure conditions induced moderate elevation of antibody production only in male mice.

Irradiation with electromagnetic waves (8.15-18 GHz, 1 Hz within, 1 microW/cm2) in vivo increases the cytotoxic activity of natural killer cells of rat spleen (Fesenko et al, 1999a). In mice exposed for 24-72 h, the activity of natural killer cells increased by 130-150%, the increased level of activity persisting within 24 h after the cessation of treatment. Microwave irradiation of animals in vivo for 3.5 and 5 h, and a short exposure of splenic cells in vitro did not affect the activity of natural killer cells.

Whole body microwave sinusoidal irradiation of male NMRI mice with 8.15-18 GHz (1 Hz within) at a power density of 1 microW/cm2 caused a significant enhancement of TNF production in peritoneal macrophages and splenic T lymphocytes (Fesenko et al, 1999b). Microwave radiation affected T cells, facilitating their capacity to proliferate in response to mitogenic stimulation. The exposure duration necessary for the stimulation of cellular immunity ranged from 5 h to 3 days. Chronic irradiation of mice for 7 days produced the decreasing of TNF production in peritoneal macrophages. The exposure of mice for 24 h increased the TNF production and immune proliferative response, and these stimulatory effects persisted over 3 days after the termination of exposure. Microwave treatment increased the endogenously produced TNF more effectively than did lipopolysaccharide, one of the most potential stimuli of synthesis of this cytokine. Microwaves, thus, indeed can be a factor interfering with the process of cell immunity!

Gapeev et al. (1996) reported that low-intensity electromagnetic radiation of extremely high frequency in the near field of modified the acitivity of mouse peritoneal neutrophils in a quasi-reasonance fashion., He compared the effect of radiation from various types of antennae, including one which created a_uniform spatial distribution of specific absorbed rating in the frequency range used and wide-band matching with the object both in near field and far field zones of the radiator. The authors extremely high frequency in near field zone but not the far field zone of the channel radiator modified the activity of mouse peritoneal neutrophils on a quasi-resonance manner. The interaction of electromagnetic radiation with the biological object has been revealed in the narrow-band frequencies of 41.8-42.05 GHz and consists in inhibition of luminol-dependent chemiluminescence of neutrophils activated by opsonized zymosan. It is not found any frequency dependence of the electromagnetic radiation effects in the far field zone of the radiator. The results obtained suggest, that the quasi-resonance dependence of the biological effect on the frequency of the electromagnetic radiation in the near field zone is conditioned by structure and nature of the electromagnetic radiation in this zone.

In 2003, Gatta et al. studied the effects of in vivo exposure to GSM-modulated 900 MHz radiation on mouse peripheral lymphocytes. The aim of this study was to evaluate whether daily whole-body exposure to 900 MHz GSM-modulated radiation could affect spleen lymphocytes. C57BL/6 mice were exposed 2 h/day for 1, 2 or 4 weeks in a TEM cell to an SAR of 1 or 2 W/kg. Untreated and sham-exposed groups were also examined. At the end of the exposure, mice were killed humanely and spleen cells were collected. The number of spleen cells, the percentages of B and T cells, and the distribution of T-cell subpopulations (CD4 and CD8) were not altered by the exposure. T and B cells were also stimulated ex vivo using specific monoclonal antibodies or LPS to induce cell proliferation, cytokine production and expression of activation markers. The results did not show relevant differences in either T or B lymphocytes from mice exposed to an SAR of 1 or 2 W/kg and sham-exposed mice with few exceptions. After 1 week of exposure to 1 or 2 W/kg, an increase in IFN-gamma (Ifng) production was observed that was not evident when the exposure was prolonged to 2 or 4 weeks. This suggests that the immune system might have adapted (!) to RF radiation as it does with other stressing agents. All together, from their in vivo data, they made the conclusion that it indicated that the T- and B-cell compartments were not substantially affected by exposure to RF radiation and that a clinically relevant effect of RF radiation on the immune system is unlikely to occur. Another explanation could be that the cells were unable to deal with the exposure and the obvious follow-up question then will be: What happened with the immune cells after months and years of exposure?

On the other hand, Kolomytseva et al. (2002), in their whole-body exposure experiment designed to study the dynamics of leukocyte number and functional activity of peripheral blood neutrophils under whole-body exposure of healthy mice to low-intensity extremely-high-frequency electromagnetic radiation (EHF EMR, 42.0 GHz, 0.15 mW/cm2, 20 min daily), showed that such a whole-body exposure of healthy mice to low-intensity EHF EMR has a profound effect on the indices of nonspecific immunity. It was shown that the phagocytic activity of peripheral blood neutrophils was suppressed by about 50% ($p<0.01$ as compared with the sham-exposed control) in 2-3 h after the single exposure to EHF EMR. The effect persisted for 1 day after the exposure, and then the phagocytic activity of neutrophils returned to the norm within 3 days. A significant modification of the leukocyte blood profile in mice exposed to EHF EMR for 5 days was observed after the cessation of exposures: the number of leukocytes increased by 44% ($p<0.05$ as compared with sham-exposed animals), mostly due to an increase in the lymphocyte content. The supposition was made that EHF EMR effects can be mediated via the metabolic systems of arachidonic acid and the stimulation of adenylate cyclase activity, with subsequent increase in the intracellular cAMP level.

The modification of indices of the humoral immune response to thymus-dependent antigen (sheep erythrocytes) after a whole-body exposure of healthy mice to low-intensity extremely-high-frequency electromagnetic radiation was reported by Lushnikov et al. in 2001. Male NMRI mice were exposed in the far-field zone of horn antenna at a frequency of 42.0 GHz and energy flux density of 0.15 mW/cm2 under different regimes: once for 20 min, for 20 min daily during 5 and 20 successive days before immunization, and for 20 min daily during 5 successive days after immunization throughout the development of the humoral immune response. The intensity of the humoral immune response was estimated on day 5 after immunization

by the number of antibody-forming cells of the spleen and antibody titers. Changes in cellularity of the spleen, thymus and red bone marrow were also assessed. The indices of humoral immunity and cellularity of lymphoid organs changed insignificantly after acute exposure and series of 5 exposures before and after immunization of the animals. However, after repeated exposures for 20 days before immunization, a statistically significant reduction of thymic cellularity by 17.5% ($p<0.05$) and a decrease in cellularity of the spleen by 14.5% ($p<0.05$) were revealed. The results show that low-intensity extremely-high-frequency electromagnetic radiation with the frequency and energy flux density used does not influence the humoral immune response intensity in healthy mice but influences immunogenesis under multiple repeated exposures.

The immunoglobulins' concentrations and T lymphocyte subsets during occupational exposures to microwave radiation were assessed in 1999 by Moszczynski et al. In the workers of retransmission TV center and center of satellite communications on increased IgG and IgA concentration and decreased count of lymphocytes and T8 cells was found. However, in the radar operators IgM concentration was elevated and a decrease in the total T8 cell count was observed. The different behaviour of examined immunological parameters indicate that the effect of microwave radiation on immune system depends on character of an exposure. Disorders in the immunoglobulins' concentrations and in the T8 cell count did not cause any reported clinical consequences.

Experiments have also been conducted to elucidate the effects of chronic low power-level microwave radiation on the immunological systems of rabbits (Nageswari et al, 1991). Fourteen male Belgian white rabbits were exposed to microwave radiation at 5 mW/cm2, 2.1 GHz, 3 h daily, 6 days/week for 3 months in two batches of 7 each in specially designed miniature anechoic chambers. Seven rabbits were subjected to sham exposure for identical duration. The microwave energy was provided through S band standard gain horns connected to a 4K3SJ2 Klystron power amplifier. The first batch of animals were assessed for T lymphocyte-mediated cellular immune response mechanisms and the second batch of animals for B lymphocyte-mediated humoral immune response mechanisms. The peripheral blood samples collected monthly during microwave/sham exposure and during follow-up (5/14 days after termination of exposures, in the second batch animals only) were analysed for T lymphocyte numbers and their mitogen responsiveness to ConA and PHA. Significant suppression of T lymphocyte numbers was noted in the microwave group at 2 months (p less than 0.01) and during follow-up (p less than 0.01). The first batch animals were initially sensitised with BCG and challenged with tuberculin (0.03 ml) at the termination of microwave irradiation/sham exposure and the increase in foot pad thickness (delta mm), which is a measure of T cell-mediated immunity (delayed type hypersensitivity response, DTH) was noted in both the groups. The microwave group revealed a more robust response than the control group (delta % +12.4 vs. +7.54).

Nakamura et al. (1997) reported on the effect of microwaves on pregnant rats. The authors reported that microwaves at the power of 10 mW/cm2 produced activation of the hypothalamic-pituitary-adrenal axis and increased oestradiol in both virgin and pregnant rats, suggesting that microwaves greatly stress pregnant organisms. Earlier data had indicated that these microwaves produce various detrimental changes based on actions of heat or non-specific stress, although the effects of microwaves on

pregnant organisms was not uniform. This study was therefore designed to clarify the effect of exposure to microwaves during pregnancy on endocrine and immune functions. Natural killer cell activity and natural killer cell subsets in the spleen were measured, as well as some endocrine indicators in blood--corticosterone and adrenocorticotrophic hormone (ACTH) as indices of the hypothalamic-pituitary-adrenal axis--beta-endorphin, oestradiol, and progesterone in six female virgin rats and six pregnant rats (nine to 11 days gestation) exposed to microwaves at 10 mW/cm2 incident power density at 2,450 MHz for 90 minutes. The same measurements were performed in control rats (six virgin and six pregnant rats). Skin temperature in virgin and pregnant rats increased immediately after exposure to microwaves. Although splenic activity of natural killer cells and any of the subset populations identified by the monoclonal antibodies CD16 and CD57 did not differ in virgin rats with or without exposure to microwaves, pregnant rats exposed to microwaves showed a significant reduction of splenic activity of natural killer cells and CD16+CD57-. Although corticosterone and ACTH increased, and oestradiol decreased in exposed virgin and pregnant rats, microwaves produced significant increases in beta-endorphin and progesterone only in pregnant rats.

Nakamura et al. (1998) evaluated the involvement of opioid systems in reduced natural killer cell activity (NKCA) in pregnant rats exposed to microwaves at a relatively low level (2 mW/cm2 incident power density at 2,450 MHz for 90 min). They assayed beta-endorphin (betaEP) in blood, pituitary lobes, and placenta as well as splenic NKCA in virgin and/or pregnant rats. Although microwaves elevated colonic temperatures by 0.8 degrees C for virgin and 0.9 degrees C for pregnant rats, and betaEP in blood and anterior pituitary lobes (AP) significantly, it did not change blood corticosterone as an index of hypothalamic-pituitary adrenal axis. There were significant interactions between pregnancy and microwave exposure on splenic NKCA, betaEP in both blood and AP, and blood progesterone. Intra-peritoneal administration of opioid receptor antagonist naloxone prior to microwave exposure increased NKCA, blood, and placental betaEP in pregnant rats. Alterations in splenic NKCA, betaEP and progesterone in pregnant rats exposed to microwaves may be due to both thermal and non-thermal actions. These results suggest that NKCA reduced by microwaves during pregnancy is mediated by the pituitary opioid system.

To further clarify the effects of microwaves on pregnancy, Nakamura et al. (2000) investigated rats exposed to continuous-wave (CW) microwave at 2 mW/cm(2) incident power density at 2,450 MHz for 90 min.. The effects on uterine or uteroplacental blood flow and endocrine and biochemical mediators, including corticosterone, estradiol, prostaglandin E(2) (PGE(2)), and prostaglandin F(2)alpha (PGF(2)alpha) were measured, –Colonic temperature in virgin and pregnant rats was not significantly altered by microwave treatment. Microwaves decreased uteroplacental blood flow and increased progesterone and PGF(2)alpha in pregnant, but not in virgin rats. Intraperitoneal (i.p.) administration of angiotensin II, a uteroplacental vasodilator, before microwave exposure prevented the reduction in uteroplacental blood flow and the increased progesterone and PGF(2)alpha in pregnant rats. Increased corticosterone and decreased estradiol during microwave exposure were observed independent of pregnancy and pretreatment with angiotensin II. These results suggest that microwaves (CW, 2 mW/cm(2), 2,450 MHz) produce uteroplacental circulatory disturbances and ovarian and placental dysfunction during pregnancy, probably through non-thermal actions. The uteroplacental disturbances

appear to be due to actions of PGF(2)alpha and may pose some risk for pregnancy. Reported pregnancy losses in women (Lee, 2001; Li, 2001) and infertility (Magras and Xenos, 1997) might be related to these laboratory findings.

Nasta et al. (2006), very recently examined the effects of in vivo exposure to a GSM-modulated 900 MHz RF field on B-cell peripheral differentiation and antibody production in mice. Their results show that exposure to a whole-body average specific absorption rate (SAR) of 2 W/kg, 2 h/day for 4 consecutive weeks does not affect the frequencies of differentiating transitional 1 (T1) and T2 B cells or those of mature follicular B and marginal zone B cells in the spleen. IgM and IgG serum levels are also not significantly different among exposed, sham-exposed and control mice. B cells from these mice, challenged in vitro with LPS, produce comparable amounts of IgM and IgG. Moreover, exposure of immunized mice to RF fields does not change the antigen-specific antibody serum level. Interestingly, not only the production of antigen-specific IgM but also that of IgG (which requires T-B-cell interaction) is not affected by RF-field exposure. This indicates that the exposure does not alter an ongoing in vivo antigen-specific immune response. In conclusion, the results of Nasta et al. (2006) do not indicate any effects of GSM-modulated RF radiation on the B-cell peripheral compartment and antibody production.

Whole-body microwave sinusoidal irradiation of male NMRI mice, exposure of macrophages in vitro, and preliminary irradiation of culture medium with 8.15-18 GHz (1 Hz within) at a power density of 1 microW/cm2 caused a significant enhancement of tumor necrosis factor production in peritoneal macrophages (Novoselova et al, 1998). The role of microwaves as a factor interfering with the process of cell immunity must, thus, be seriously considered. Furthermore the effect of 8.15-18 GHz (1 Hz within) microwave radiation at a power density of 1 microW/cm2 on the tumor necrosis factor (TNF) production and immune response was tested by Novoselova et al. (1999). A single 5 h whole-body exposure induced a significant increase in TNF production in peritoneal macrophages and splenic T cells. The mitogenic response in T lymphocytes increased after microwave exposure. The activation of cellular immunity was observed within 3 days after exposure. The diet containing lipid-soluble nutrients (beta-carotene, alpha-tocopherol and ubiquinone Q9) increased the activity of macrophages and T cells from irradiated mice.

Obukhan (1998) has performed cytologic investigations designed to study bone marrow, peripheral blood, spleen, and thymus of albino rats irradiated by an electromagnetic field, 2,375, 2,450, and 3,000 MHz. Structural and functional changes in populations of megakaryocytes, immunocompetent cells as well as of undifferentiated cells, and of other types of cells that are dependent on the intensity of irradiation.

The possibility of genotoxicity of radiofrequency radiation (RFR) applied alone or in combination with x-rays was recently investigated in vitro using several assays on human lymphocytes by Stronati and colleagues (2006). The chosen specific absorption rate (SAR) values are near the upper limit of actual energy absorption in localized tissue when persons use some cellular telephones. The purpose of the combined exposures was to examine whether RFR might act epigenetically by reducing the fidelity of repair of DNA damage caused by a well-characterized and

established mutagen. Blood specimens from 14 donors were exposed continuously for 24 h to a Global System for Mobile Communications (GSM) basic 935 MHz signal. The signal was applied at two SAR; 1 and 2 W/Kg, alone or combined with a 1-min exposure to 1.0 Gy of 250 kVp x-rays given immediately before or after the RFR. The assays employed were the alkaline comet technique to detect DNA strand breakage, metaphase analyses to detect unstable chromosomal aberrations and sister chromatid exchanges, micronuclei in cytokinesis-blocked binucleate lymphocytes and the nuclear division index to detect alterations in the speed of in vitro cell cycling. By comparison with appropriate sham-exposed and control samples, no effect of RFR alone could be found for any of the assay endpoints. In addition RFR did not modify any measured effects of the x-radiation. In conclusion, this study has used several standard in vitro tests for chromosomal and DNA damage in Go human lymphocytes exposed in vitro to a combination of x-rays and RFR. It has comprehensively examined whether a 24-h continuous exposure to a 935 MHz GSM basic signal delivering SAR of 1 or 2 W/Kg is genotoxic per se or whether, it can influence the genotoxicity of the well-established clastogenic agent; x-radiation. Within the experimental parameters of the study in all instances no effect from the RFR signal was observed.

Tuschl et al. (1999) recorded a considerable excess of recommended exposure limits in the vicinity of shortwave diathermy devices used for medical treatment of patients. Different kinds of field probes were used to measure electric and magnetic field strength and the whole body exposure of medical personnel operating shortwave, decimeter wave and microwave units was calculated. To investigate the influence of chronic exposure on the immune system of operators, blood was sampled from physiotherapists working at the above mentioned devices. Eighteen exposed and thirteen control persons, matched by sex and age, were examined. Total leucocyte and lymphocyte counts were performed and leucocytic subpopulations determined by flow cytometry and monoclonal antibodies against surface antigens. In addition, to quantify subpopulations of immunocompetent cells, the activity of lymphocytes was measured. Lymphocytes were stimulated by mitogen phytohemagglutinin and their proliferation measured by a flow cytometric method. No statistically significant differences between the control and exposed persons were found. In both study groups all immune parameters were within normal ranges.

Despite the important role of the immune system in defending the body against infections and cancer, only few investigations on possible effects of radiofrequency (RF) radiation on function of human immune cells have been undertaken. One of these is the investigation by Tuschl et al. in 2005 where they assessed whether GSM modulated RF fields have adverse effects on the functional competence of human immune cells. Within the frame of the multidisciplinary project "Biological effects of high frequency electromagnetic fields (EMF)" sponsored by the National Occupation Hazard Insurance Association (AUVA) in vitro investigations were carried out on human blood cells. Exposure was performed at GSM Basic 1950 MHz, an SAR of 1 mW/g in an intermittent mode (5 min "ON", 10 min "OFF") and a maximum Delta T of 0.06 degrees C for the duration of 8 h. The following immune parameters were evaluated: (1) the intracellular production of interleukin-2 (IL-2) and interferon (INF) gamma in lymphocytes, and IL-1 and tumor necrosis factor (TNF)-alpha in monocytes were evaluated with monoclonal antibodies. (2) The activity of immune-relevant genes (IL 1-alpha and beta, IL-2, IL-2-receptor, IL-4, macrophage colony stimulating factor (MCSF)-receptor, TNF-alpha, TNF-alpha-receptor) and

housekeeping genes was analyzed with real time PCR. (3) The cytotoxicity of lymphokine activated killer cells (LAK cells) against a tumor cell line was determined in a flow cytometric test. For each parameter, blood samples of at least 15 donors were evaluated. No statistically significant effects of exposure were found and there is no indication that emissions from mobile phones are associated with adverse effects on the human immune system.

Irradiation by pulsed microwaves (9.4 GHz, 1 microsecond pulses at 1,000/s), both with and without concurrent amplitude modulation (AM) by a sinusoid at discrete frequencies between 14 and 41 MHz, was assessed for effects on the immune system of Balb/C mice (Veyret et al, 1991). The mice were immunized either by sheep red blood cells (SRBC) or by glutaric-anhydride conjugated bovine serum albumin (GA-BSA), then exposed to the microwaves at a low rms power density (30 microW/cm2; whole-body-averaged SAR approximately 0.015 W/kg). Sham exposure or microwave irradiation took place during each of five contiguous days, 10 h/day. The antibody response was evaluated by the plaque-forming cell assay (SRBC experiment) or by the titration of IgM and IgG antibodies (GA-BSA experiment). In the absence of AM, the pulsed field did not greatly alter immune responsiveness. In contrast, exposure to the field under the combined-modulation condition resulted in significant, AM-frequency-dependent augmentation or weakening of immune responses.

Finally, in addition, classical allergy reactions, such as chromate allergy, has been studied by Seishima et al. (2003). The background for the study was an earlier case report about a patient with allergic contact dermatitis caused by hexavalent chromium plating on a cellular phone. The new study described the clinical characteristics and results of patch tests (closed patch tests and photopatch tests were performed using metal standard antigens) in 8 patients with contact dermatitis possibly caused by handling a cellular phone. The 8 patients were 4 males and 4 females aged from 14 to 54 years. They each noticed skin eruptions after 9-25 days of using a cellular phone. All patients had erythema, and 7 had papules on the hemilateral auricle or in the preauricular region. Three of 8 patients had a history of metal allergy. Chromate, aluminium and acrylnitrile-butadiene-styrene copolymer were used as plating on the cellular phones used by these patients. The patch test was positive for 0.5, 0.1 and 0.05% potassium dichromate in all 8 patients. The photopatch test showed the same results. One patient was positive for 2% cobalt chloride and one for 5% nickel sulfate. Based on these data, it is important to consider the possibility of contact dermatitis due to a cellular phone, possibly caused by chromate, when the patients have erythema and papules on the hemilateral auricle or in the preauricular region.

VII. Electromagnetic fields and health

Since the formation of life on Earth, as we know it, more than 3.5 billion years ago, the only real source of radiation, apart from Earth's static geomagnetic field, has been the sun. All living organisms that have evolved and not been able to cope with it are either gone or have adapted to it in one of several ways. Living under-ground, only being active during night, living in the deeper waters (1 meter or deeper) in oceans and lakes, under the foliage of jungle-trees, or - as all day-active organisms have – developed a skin (or, for plants, a cortex) containing a pigment (animals and plants have very similar ones) that will shield some heat and some sunshine…but not very

much. Any fair-skinned Irish or Scandinavian person learns very early to avoid even the rather bleak sun up-north, because – if not – you will easily get a nasty sunburn. Later on, that sunburn will develop into a postinflammatory hyperpigmentation, with it's cosmetic values, however, well before it you will get a strong alarm signal in the form of a redness of the skin.

When considering other frequencies, the pigment does not furnish any protection at all, something mankind has found out during the last 100 years. Cosmic rays, radioactivity, X-rays, UVC, UVB and now even UVA are considered, together with radar-type microwaves to be very, or even extremely, dangerous to your health. You are translucent to exposures such as power-frequent magnetic fields as well as mobile phone and WI-FI microwaves, but this does not mean that they are without possible effect, through thermal or non-thermal mechanisms.

Is it possible that we can adapt our biology to altered exposure conditions in less than 100 years, or do we have to have thousands of years for such an adaptation? And, in the meantime, what kind of safety standards must we adopt if the current public safety limits are not sufficiently protective of public health?

The World Health Organization (WHO) has acknowledged the condition of electrohypersensitivity, and published a 2006 research agenda for radio-frequency fields (see Addendum to Chapter 12 on the Swedish Government response to persons with Electrosensitivity). The WHO recommends that people reporting sensitivities receive a comprehensive health evaluation. It states: "Some studies suggest that certain physiological responses of EHS individuals tend to be outside the normal range. In particular, hyperactivity in the central nervous system and imbalance in the autonomic nervous system need to be followed up in clinical investigations and the results for the individuals taken as input for possible treatment." Studies of individuals with sensitivities ought to consider sufficient acclimatization of subjects as recommended for chemical sensitivities, as well as recognition of individuals' wavelength-specific sensitivities. Reduction of electromagnetic radiation may ameliorate symptoms in people with chronic fatigue.

Off-gassing of electrical equipment may also contribute to sensitivities. Different sorts of technology (e.g. various medical equipment, analogue or digital telephones; flat screen monitors and laptop computers or larger older monitors) may vary significantly in strength, frequency and pattern of electromagnetic fields. One challenging question for science is to find out if, for instance, 50- or 60-Hz ELF pure sine wave, square waves or sawtooth waveform, ELF-dirty (e.g. radiofrequencies on power lines), ELF-modulated radiofrequency fields, continuous wave radiofrequency radiation and particularly pulsed radiofrequency signals are more or less bioactive, e.g. as neurotoxic and/or carcinogenic environmental exposure parameters. (see Chapter 8 on Disruption by Modulation).

VIII. Conclusions

• Both human and animal studies report large immunological changes with exposure to environmental levels of electromagnetic fields (EMFs). Some of these exposure levels are equivalent to those of e.g. wireless technologies in daily life.

• Measurable physiological changes (mast cells increases, for example) that are bedrock indicators of allergic response and inflammatory conditions are stimulated by EMF exposures.

• Chronic exposure to such factors that increase allergic and inflammatory responses on a continuing basis may be harmful to health.

• It is possible that chronic provocation by exposure to EMF can lead to immune dysfunction, chronic allergic responses, inflammatory responses and ill health if they occur on a continuing basis over time. This is an important area for future research.

• Specific findings from studies on exposures to various types of modern equipment and/or EMFs report over-reaction of the immune system; morphological alterations of immune cells; profound increases in mast cells in the upper skin layers, increased degranulation of mast cells and larger size of mast cells in electrohypersensitive individuals; presence of biological markers for inflammation that are sensitive to EMF exposure at non-thermal levels; changes in lymphocyte viability; decreased count of NK cells; decreased count of T lymphocytes; negative effects on pregnancy (uteroplacental circulatory disturbances and placental dysfunction with possible risks to pregnancy); suppressed or impaired immune function; and inflammatory responses which can ultimately result in cellular, tissue and organ damage.

• Electrical hypersensitivity is reported by individuals in the United States, Sweden, Switzerland, Germany. Denmark and many other countries of the world. Estimates range from 3% to perhaps 10% of populations, and appears to be a growing condition of ill-health leading to lost work and productivity.

• The WHO and IEEE literature surveys do not include all of the relevant papers cited here, leading to the conclusion that evidence has been ignored in the current WHO ELF Health Criteria Monograph; and the proposed new IEEE C95.1 RF public exposure limits (April 2006).

• The current international public safety limits for EMFs do not appear to be sufficiently protective of public health at all, based on the studies of immune function. New, biologically-based public standards are warranted that take into account low-intensity effects on immune function and health that are reported in the scientific

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Appendix 8-A Some legal aspects of the functional impairment electrohypersensitivity in Sweden

In Sweden, electrohypersensitivity (EHS) is an officially fully recognized functional impairment (i.e., it is not regarded as a disease). Survey studies show that somewhere between 230,000 - 290,000 Swedish men and women, out of a population of 9,000,000 people, report a variety of symtoms when being in contact with electromagnetic field (EMF)-sources.

The electrohypersensitive persons have their own handicap organisation; The Swedish Association for the ElectroSensitive; http://www.feb.se (the website has an English version). This organisation is included in the Swedish Disability Federation (Handikappförbundens SamarbetsOrgan; HSO). HSO is the unison voice of the Swedish disability associations towards the government, the parliament and national authorities and is a cooperative body that today consists of 43 national disability organisations (where The Swedish Association for the ElectroSensitive is 1 of these 43 organisations) with all together about 500,000 individual members. You can read more on http://www.hso.se (the site has an English short version). The Swedish Association for the ElectroSensitive gets a governmental subsidy as a handicap organization according to SFS 2000:7 §2 (SFS = The Swedish Governmental Statute-Book). EHS persons' right to get disablement allowances has been settled in The Swedish Supreme Administrative Court, i.a. in the judgement "dom 2003-01-29, mål nr. 6684-2001".

Swedish municipalities, of course, have to follow the UN 22 Standard Rules on the equalization of opportunities for persons with disabilities ("Standardregler för att tillförsäkra människor med funktionsnedsättning delaktighet och jämlikhet"; about the UN 22 Standard Rules, see website: http://www.un.org/esa/socdev/enable/dissre00.htm). All persons with disabilities shall, thus, be given the assistance and service they have the right to according to the Swedish Act concerning Support and Service for Persons with Certain Functional Impairments (LSS-lagen) and the Swedish Social Services Act (Socialtjänstlagen). Persons with disabilities, thus, have many different rights and can get different kinds of support. The purpose of those rights and the support is to give every person the chance to live like everyone else. Everyone who lives in the Swedish municipalities should be able to lead a normal life and the municipalities must have correct knowledge and be able to reach the persons who need support and service. Persons with disabilities shall be able to get extra support so that they can live, work, study, or do things they enjoy in their free time. The municipalities are responsible for making sure that everyone gets enough support. Everyone shall show respect and remember that such men and women may need different kinds of support.

In Sweden, impairments are viewed from the point of the environment. No human being is in itself impaired, there are instead shortcomings in the environment that cause the impairment (as the lack of ramps for the person in a wheelchair or rooms electrosanitized for the person with electrohypersensitivity). This environment-related impairment view, furthermore, means that even though one does not have a scientifically-based complete explanation for the impairment electrohypersensitivity, and in contrast to disagreements in the scientific society, the person with

electrohypersensitivity shall always be met in a respectful way and with all necessary support with the goal to eliminate the impairment. This implies that the person with electrohypersensitivity shall have the opportunity to live and work in an electrosanitized environment.

This view can fully be motivated in relation to the present national and international handicap laws and regulations, including the UN 22 Standard Rules and the Swedish action plan for persons with impairments (prop. 1999/2000:79 "Den nationella handlingplanen för handikappolitiken - Från patient till medborgare"). Also the Human Rights Act in the EU fully applies.

A person is disabled when the environment contains some sort of impediments. It means that in that moment a man or woman in a wheelchair can not come onto the bus, a train, or into a restaurant, this person has a disability, he or she is disabled. When the bus, the train or the restaurant are adjusted for a wheelchair, the person do not suffer from his disability and are consequently not disabled. An electrohypersensitive person suffers when the environment is not properly adapted according to their personal needs. Strategies to enable a person with this disability to attend common rooms such as libraries, churches and so on, are for instance to switch off the high-frequency fluorescent lamps and instead use ordinary light bulbs. Another example is the possibility to switch off - the whole or parts of - the assistive listening systems (persons with electrohypersensitivity are often very sensitive to assistive listening systems).

In the Stockholm municipality - were I live and work as a scientist with the responsibility to investigate comprehensive issues for persons with electrohypersensitivity - such persons have the possibility to get their home sanitized for EMFs. It means for example that ordinary electricity cables are changed to special cables. Furthermore, the electric stove can be changed to a gas stove and walls, roof and floors can be covered with special wallpaper or paint with a special shelter to stop EMFs from the outside (from neighbours and mobile telephony base stations). Even the windows can be covered with a thin aluminum foil as an efficient measure to restrain EMFs to get into the room/home. If these alterations turn out not to be optimal they have the possibility to rent small cottages in the countryside that the Stockholm municipality owns. These areas have lower levels of irradiation than others. The Stockholm municipality also intend to build a village with houses that are specially designed for persons who are electrohypersensitive. This village will be located in a low-lewel irradiation area. [One of my graduate students, Eva-Rut Lindberg, has in her thesis project studied the "construction of buildings for persons with the impairment electrohypersensitivity". The doctoral thesis will be presented during the Autumn.]

Persons with electrohypersensitivity also have a general (legal) right to be supported by their employer so that they can work despite of this impairment. For instance, they can get special equipment such as computers that are of low-emission type, that high-frequency fluorescent lamps are changed to ordinary light bulbs, no wireless DECT telephones in their rooms, and so on.

Some hospitals in Sweden (e.g. in Umeå, Skellefteå and Karlskoga) also have built special rooms with very low EMFs so that persons who are hypersensitive can get

medical care. Another example is the possibility for persons who are electrohypersensitive to get a specially designed car so that the person can transport himself/herself between his/her home and their workplace.

Recently, some politicians in the Stockholm municipality even proposed to the politicians responsible for the subway in the Stockholm City that a part of every trainset should be free from mobile phones; that the commuters have to switch of the phones in these selected parts to enable persons with electrohypersensitivity to travel with the subway (compare this with persons who have an allergy for animal fur whereupon people consequently is prohibited to have animals, such as dogs or cats, in selected parts of the trainset).

In addition, when the impairment electrohypersensitivity is discussed it is also of paramount importance that more general knowledge is needed with the aim to better adapt the society to the specific needs of the persons with this impairment. The Swedish "Miljöbalk" (the Environmental Code) contains an excellent prudence avoidance principle which, of course, most be brought into action also here, together with respect and willingness to listen to the persons with electrohypersensitivity.

Naturally, all initiatives for scientific studies of the impairment electrohypersensitivity must be characterized and marked by this respect and willingness to listen, and the investigations shall have the sole aim to help the persons with this particular impairment. Rule 13 in the UN 22 Standard Rules clearly says that scientific investigations of impairments shall, in an unbiased way - and without any prejudice - focus on cause, occurrence and nature and with the sole and explicit purpose to help and support the person with the impairment.

A unique conference recently was held in Stockholm in May, 2006. The theme for the conference was "The right for persons with the impairment electrohypersensitivity to live in a fully accessible society". The conference was organized by the Stockholm City municipality and the Stockholm County Council and dealt with the most recent measures to make Stockholm fully accessible for persons with the impairment electrohypersensitivity. Among such measures are to offer home equipment adjustments, ban mobile phones from certain underground cars as well as certain public bus seats, and through electrosanitized hospital wards. The conference was documented on film.

SECTION 9

EVIDENCE FOR EFFECTS ON

NEUROLOGY AND BEHAVIOR

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Appendix 9-B - Memory and Behavior: The Biological Effects, Health Consequences and Standards for Pulsed Radiofrequency Field. International Commission on Nonionizing Radiation Protection and the World Health Organization, Ettoll Majorare, Centre for Scientific Culture, Italy, 1999.

I. Introduction

This chapter is a brief review of recent studies on the effects of radiofrequency radiation (RFR) on neuronal functions and their implication on learning and memory in animal studies, effects on electrical activity of the brain and relation to cognitive functions, and finally a section on the effects of cell phone radiation on the auditory system. There is also a set of studies reporting subjective experience in humans exposed to RFR. This includes reports of fatigue, headache, dizziness, and sleep disturbance, etc.

The close proximity of a cellular telephone antenna to the user's head leads to the deposition of a relatively large amount of radiofrequency energy in the head. The relatively fixed position of the antenna to the head causes a repeated irradiation of a more or less fixed amount of body tissue, including the brain at a relatively high intensity to ambient levels. The question is whether such exposure affects neural functions and behavior.

II. Chemical and cellular changes

Several studies have investigated the effect of RFR on the cholinergic system because of its involvement in learning and wakefulness and animals. Testylier et al. [2002] reported modification of the hippocampal cholinergic system in rats during and after exposure to low-intensity RFR. Bartier et al. [2005] reported that RFR exposure induced structural and biochemical changes in AchE, the enzyme involved in acetylcholine metabolism. Vorobyov et al. [2004] reported that repeated exposure to low-level extremely low frequency-modulated RFR affected baseline and scopolamine-modified EEG in freely moving rats. However, recently Crouzier et al [2007] found no significant change in acetylcholine-induced EEG effect in rats exposed for 24 hours to a 1.8 MHz GSM signal at 1.2 and 9 W/cm^2.

There are several studies on the inhibitory and excitatory neurotransmitters. A decrease in GABA, an inhibitory transmitter, content in the cerebellum was reported by Mausset et al. [2001] after exposure to RFR at 4 W/kg. The same researchers [Maussset-Bonnefont et al., 2004] also reported changes in affinity and concentration of NMDA and GABA receptors in the rat brain after an acute exposure at 6 W/kg. Changes in GABA receptors has also been reported by Wang et al. [2005], and reduced excitatory synaptic activity and number of excitatory synapses in cultured rat hippocampal neurons have been reported by Xu et al. [2006] after RFR exposure. Related to the findings of changes in GABA in the brain is that RFR has been shown to facilitate seizure in rats given subconvulsive doses of picotoxin, a drug that blocks the GABA system [Lopez Martin et al., 2006]. This finding raises the concern that humans with epileptic disorder could be more susceptible to RFR exposure.

Not much has been done on single cell in the brain after RFR exposure. Beason and Semm [2002] reported changes in the amount of neuronal activity by brain cells of birds exposed to GSM signal. Both increase and decrease in firing were observed. Salford et al. [2003] reported cellular damage and death in the brain of rat after acute exposure to GSM signals. Tsurita et al. [2000] reported no significant morphological change in the cerebellum of rats exposed for 2-4