0000159019

RECEIVED

2014 DEC 22 P 3: 29

CORP COMMISSION
DOCKET CONTROL

Transcript Exhibit(s)

Docket No(s): E-00000C-11-0328

Arizona Corporation Commission
DOCKETED
DEC 22 2014
DOCKETED BY

ORIGINAL

Exhibit #: 1, 2

Volume 16, issues 2–3, August 2009

ISSN 0928-4680

EXHIBIT

PENGAD 800-631-6989

ISP

INTERNATIONAL SOCIETY for PATHOPHYSIOLOGY

PATHOPHYSIOLOGY

The Official Journal of the International Society for Pathophysiology

Editor-in-Chief:
O. Hänninen, Kuopio, Finland

Special Issue
Electromagnetic Fields (EMF)

Guest Editor:
Martin Blank

PATHOPHYSIOLOGY

Pathophysiology is an international journal publishing papers in English which address the etiology, development, and elimination of pathological processes. Contributions on the basic mechanisms underlying these processes, model systems and interdisciplinary approaches are strongly encouraged.

Pathophysiology has a broad scope and is managed by an international editorial board which consists of highly respected scientists from different speciality fields. As the biomedical sciences are becoming more interdisciplinary, *Pathophysiology* is eminently suitable for the publication of key articles in this field. Contributions covering the following areas are welcomed: general pathophysiological processes—inflammation, infection, hypoxia, stress, shock, pain, disregulation; cellular and molecular pathophysiology; neuroscience; heart and circulation; respiratory system; renal, fluid and electrolyte pathophysiology; gastrointestinal and hepatic system; endocrine system; metabolic disorders; blood system; immune system; reproductive system; locomotor system. The journal's audience comprises: physiologists, pathologists, physicians, neurologists, cardiologists, etc. in both university and hospital environments.

Editor-in-Chief: Osmo Hänninen, Department of Physiology, University of Kuopio, P.O. Box 1627, Fi-70211, Finland. Tel.: +358-50-5506903; Fax: +358-17-163112; E-mail: osmo.hanninen@uku.fi

Regional Editor (Americas): D. Neil Granger, Department of Molecular and Cellular Physiology, Louisiana State University Health Sciences Center, 1501 Kings Highway, Shreveport, LA 71130-3932, USA. Tel.: +1 (318) 675 6011; Fax: +1 (318) 675 6005; E-mail: dgrang@lsuhsc.edu

Regional Editor (Europe): Hans-Christoph Scholle, FB Motorik, Institute for Pathophysiology, Friedrich-Schiller-Universität Jena, Erfurter Strasse 35, 07740 Jena. Tel.: +49(0)3641937373; Fax: +49(0)3641937377; E-mail: hscho@moto.uni-jena.de

Regional Editor (Asia-Pacific): Osamu Matsuo, Kinki University School of Medicine, Osakasayama, 589-8511 Japan. Tel.: +81 72 366 0221 (ext 3163); Fax: +81 72 366 2853; E-mail: matsuo-o@med.kindai.ac.jp

Founding Editor: Toshikazu Yoskikawa, First Department of Medicine, Kyoto Prefectural University of Medicine, Kamingyo-Ku, Kyoto 602-8566 Japan.

Editorial Board

Yuri Arhipenko (Moscow, Russia)
Mustafa Atalay (Kuopio, Finland)
Reinhard Bauer (Jena, Germany)
Allen Cowley (Milwaukee, USA)
Dipak Das (Farmington, USA)
Dragan M. Djuric (Belgrade, Serbia and Montenegro)
Mustafa Gul (Erzurum, Turkey)
Yves Henrotin (Liege, Belgium)
Ilpo Huhtaniemi (London, UK)
Malcolm Jackson (Liverpool, UK)
Sushil Jain (Shreveport, Louisiana, USA)
Ronald J. Korthuis (Columbia, MO, USA)
Boris Krylov (St. Petersburg, Russia)
George N. Kryzhanovsky (Moscow, Russia)
Esko Länsimies (Kuopio, Finland)
Wenhua Ling (Guangzhou, China)
Amanda Lochner (Tygerberg, South Africa)
Jian Lu (Shanghai, China)
Emil Monos (Budapest, Hungary)
Yutaka Oomura (Toyama, Japan)
Sergei Orlov (Montreal, Canada)
Antonio Rendas (Lisbon, Portugal)
Laszlo Rosivall (Budapest, Hungary)
Toshiie Sakata (Fukuoka, Japan)
Chandan K. Sen (Columbus, Ohio, USA)
Karen Y. Stokes (Shreveport, Louisiana, USA)
Daniel L. Traber (Galveston, Texas, USA)
Weikang Wu (Guangzhou, China)
Youyi Zhang (Beijing, China)

Pathophysiology is the official journal of the International Society for Pathophysiology. Members of this international society can enter a personal subscription to the journal at a special rate through the society. Membership enquiries should be addressed to the Secretary General of the ISP, Youyi Zhang, Institute of Vascular Medicine, Peking University Third Hospital No. 49, North Garden Road, Haidian District, Beijing 10083, China. Tel.: (+86) (10) 82802306, E-mail: zhangyy@bjmu.edu.cn

Publication information: *Pathophysiology* (ISSN 0928-4680). For 2009 volume 16 is scheduled for publication. Subscription prices are available upon request from the Publisher or from the Regional Sales Office nearest you or from this journal's website (http://www.elsevier.com/locate/pathophys). Further information is available on this journal and other Elsevier products through Elsevier's website: (http://www.elsevier.com). Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by standard mail (surface within Europe, air delivery outside Europe). Priority rates are available upon request. Claims for missing issues should be made within six months of the date of dispatch.

Author enquiries: For enquiries relating to the submission of articles (including electronic submission where available) please visit this journal's homepage at http://www.elsevier.com/locate/pathophys. You can track accepted articles at http://www.elsevier.com/trackarticle and set up e-mail alerts to inform you of when an article's status has changed. Also acessible from here is information on copyright, frequently asked questions and more.

Contact details for questions arising after acceptance of an article, especially those relating to proofs, will be provided by the publisher.

Orders, claims, and journal enquiries: please contact the Customer Service Department at the Regional Sales Office nearest you:

Orlando: Elsevier, Customer Service Department, 6277 Sea Harbor Drive, Orlando, FL 32887-4800, USA; phone: (800) 6542452 [toll free within the USA]; fax (407) 3639661; phone: (+1) (407) 5636020 [outside the USA]; fax: (+1) (407) 3631354; e-mail: JournalsCustomerService-usa@elsevier.com

Amsterdam: Elsevier, Customer Service Department, PO Box 211, 1000 AE Amsterdam, The Netherlands; phone: (+31) (20) 4853757; fax: (+31) (20) 4853432; e-mail: JournalsCustomerServiceEMEA@elsevier.com

Tokyo: Elsevier, Customer Service Department, 4F Higashi-Azabu, 1-Chome Bldg, 1-9-15 Higashi-Azabu, Minato-ku, Tokyo 106-0044, Japan; phone: (+81) (3) 5561 5037; fax: (+81) (3) 5561 5047; e-mail: JournalsCustomerServiceJapan@elsevier.com

Singapore: Elsevier, Customer Service Department, 3 Killiney Road, #08-01 Winsland House I, Singapore 239519; phone: (+65) 63490222; fax: (+65) 67331510; e-mail: JournalsCustomerServiceAPAC@elsevier.com

ISP PATHOPHYSIOLOGY

VOL. 16/2–3 (2009)

ISP
PATHOPHYSIOLOGY

Editor-in-Chief:
Osmo Hänninen
Department of Physiology
University of Kuopio
P.O. Box 1627, Fi-70211
Finland
Tel.: +358-50-5506903;
Fax: +358-17-163112;
E-mail: osmo.hanninen@uku.fi

Regional Editor (Americas):
D. Neil Granger
Department of Molecular and Cellular Physiology
Louisiana State University Health Sciences Center
1501 Kings Highway
Shreveport, LA 71130-3932
USA
Tel.: +1 (318) 675 6011;
Fax: +1 (318) 675 6005;
E-mail: dgrang@lsuhsc.edu

Regional Editor (Europe):
Hans-Christoph Scholle
FB Motorik
Institute for Pathophysiology
Friedrich-Schiller-Universität Jena
Erfurter Strasse 35
07740 Jena
Tel.: +49(0)3641937373;
Fax: +49(0)3641937377;
E-mail: hscho@moto.uni-jena.de

Regional Editor (Asia-Pacific):
Osamu Matsuo
Kinki University School of Medicine
Osakasayama
589-8511 Japan
Tel.: +81 72 366 0221 (ext 3163);
Fax: +81 72 366 2853;
E-mail: matsuo-o@med.kindai.ac.jp

Founding Editor:
Toshikazu Yoskikawa
First Department of Medicine
Kyoto Prefectural University of Medicine
Kamingyo-Ku
Kyoto 602-8566
Japan

Editorial Board
Yuri Arhipenko *(Moscow, Russia)*
Mustafa Atalay *(Kuopio, Finland)*
Reinhard Bauer *(Jena, Germany)*
Allen Cowley *(Milwaukee, USA)*
Dipak Das *(Farmington, USA)*
Dragan M. Djuric *(Belgrade, Serbia and Montenegro)*
Mustafa Gul *(Erzurum, Turkey)*
Yves Henrotin *(Liege, Belgium)*
Ilpo Huhtaniemi *(London, UK)*
Malcolm Jackson *(Liverpool, UK)*
Sushil Jain *(Shreveport, Louisiana, USA)*
Ronald J. Korthuis *(Columbia, MO, USA)*
Boris Krylov *(St. Petersburg, Russia)*
George N. Kryzhanovsky *(Moscow, Russia)*
Esko Länsimies *(Kuopio, Finland)*
Wenhua Ling *(Guangzhou, China)*
Amanda Lochner *(Tygerberg, South Africa)*
Jian Lu *(Shanghai, China)*
Emil Monos *(Budapest, Hungary)*
Yutaka Oomura *(Toyama, Japan)*
Sergei Orlov *(Montreal, Canada)*
Antonio Rendas *(Lisbon, Portugal)*
Laszlo Rosivall *(Budapest, Hungary)*
Toshiie Sakata *(Fukuoka, Japan)*
Chandan K. Sen *(Columbus, Ohio, USA)*
Karen Y. Stokes *(Shreveport, Louisiana, USA)*
Daniel L. Traber *(Galveston, Texas, USA)*
Weikang Wu *(Guangzhou, China)*
Youyi Zhang *(Beijing, China)*

Cited in Excerpta Medica (EMBASE)

ISP PATHOPHYSIOLOGY

The Official Journal of the International Society for Pathophysiology

VOL. 16 (2009)

Editor-in-Chief: O. Hänninen

ELSEVIER

Amsterdam—Boston—Jena—London—New York—Oxford—Paris—Philadelphia—San Diego—St. Louis

© [2009] Elsevier Ireland Ltd. All rights reserved.

This journal and the individual contributions contained in it are protected under copyright by Elsevier Ireland Ltd., and the following terms and conditions apply to their use:

Photocopying
Single photocopies of single articles may be made for personal use as allowed by national copyright laws. Permission of the Publisher and payment of a fee is required for all other photocopying, including multiple or systematic copying, copying for advertising or promotional purposes, resale, and all forms of document delivery. Special rates are available for educational institutions that wish to make photocopies for non-profit educational classroom use.

For information on how to seek permission visit www.elsevier.com/permissions or call: (+44) 1865 843830 (UK) / (+1) 215 239 3804 (USA).

Derivative Works
Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution. Permission of the Publisher is required for all other derivative works, including compilations and translations (please consult www.elsevier.com/permissions).

Electronic Storage or Usage
Permission of the Publisher is required to store or use electronically any material contained in this journal, including any article or part of an article (please consult www.elsevier.com/permissions).
Except as outlined above, no part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without prior written permission of the Publisher.

Notice
No responsibility is assumed by the Publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made.
Although all advertising material is expected to conform to ethical (medical) standards, inclusion in this publication does not constitute a guarantee or endorsement of the quality or value of such product or of the claims made of it by its manufacturer.

ISP
PATHOPHYSIOLOGY

The Official Journal of the International Society for Pathophysiology

Special Issue:
Electromagnetic Fields (EMF)

Guest Editor:
Martin Blank

Vol. 16, Issues 2–3 AUGUST 2009

ISP
PATHOPHYSIOLOGY

Contents

Cited in EMBASE/Excerpta Medica

Preface
M. Blank (USA) 67

EMF Effects on DNA
Electromagnetic fields stress living cells
M. Blank and R. Goodman (USA) 71
Electromagnetic fields and DNA damage
J.L. Phillips, N.P. Singh and H. Lai (USA) 79
Genotoxic effects of radiofrequency electromagnetic fields
H.W. Ruediger (Austria) 89

EMF Effects on the Brain
Increased blood–brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone
H. Nittby, A. Brun, J. Eberhardt, L. Malmgren, B.R.R. Persson and L.G. Salford (Sweden) 103
Epidemiological evidence for an association between use of wireless phones and tumor diseases
L. Hardell, M. Carlberg and K. Hansson Mild (Sweden) 113
Mobile phone base stations—Effects on wellbeing and health
M. Kundi and H.-P. Hutter (Austria) 123
Estimating the risk of brain tumors from cellphone use: Published case–control studies
L.L. Morgan (USA) 137

EMF in the Environment
Long-term exposure to magnetic fields and the risks of Alzheimer's disease and breast cancer: Further biological research
Z. Davanipour and E. Sobel (USA) 149
Disturbance of the immune system by electromagnetic fields—A potentially underlying cause for cellular damage and tissue repair reduction which could lead to disease and impairment
O. Johansson (Sweden) 157
Reproductive and developmental effects of EMF in vertebrate animal models
A.F. Pourlis (Greece) 179

(Contents continued on page 249)

The table of contents of *Pathophysiology* is included in ESTOC — Elsevier Tables of Contents service — which can be accessed on the World Wide Web at the following URL addresses:
http://www.elsevier.com/locate/estoc

0928-4680(200908)16:2/3;1-2

05121

(Contents continued from outside back cover)

Electromagnetic pollution from phone masts. Effects on wildlife
A. Balmori (Spain) 191
FM-radio and TV tower signals can cause spontaneous hand movements near moving RF reflector
P. Huttunen, O. Hänninen and R. Myllylä (Finland) 201
Cell phone radiation: Evidence from ELF and RF studies supporting more inclusive risk identification and assessment
C. Blackman (USA) 205

Science as a Guide to Public Policy
Late Lessons from Early Warnings: Towards realism and precaution with EMF?
D. Gee (Denmark) 217
Public health implications of wireless technologies
C. Sage and D.O. Carpenter (USA) 233
The London Resolution
O. Johansson (Sweden) 247

ELSEVIER

Pathophysiology 16 (2009) 67–69

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Preface

There is an old joke with a well-known punch line about a man who has just fallen from the 86th floor of the Empire State Building in New York. As he passes the 30th floor, he is heard saying to himself 'so far, so good'...

Most of us laugh because we know where the man is headed, and that he must know too. But, our laughter usually has a guilty edge. We know that many of us are guilty of occasionally displaying a 'so far, so good' attitude in our own lives. We think of the smoker who says that about the possibility of getting lung cancer or heart disease and who counts on beating the odds because he feels healthy at the moment. That smoker will not find out if he won the bet until many years later, and by then it is often too late. The 'so far, so good' attitude to health is so common that people even kid themselves about it. One smoker told me that smoking would only cut a few years off his life, and that he did not mind losing the last few years because they are usually not much fun anyway.

Unlike the optimist in the joke, whose end is virtually certain, many of us live like the smoker, playing the odds and reassuring ourselves 'so far, so good'. Diseases like cancer usually take many years to develop, and we try not to think how some of the things we do casually can affect the long-term odds by compromising the natural processes that protect us. We rely on our bodies to be strong and resilient all the time. Yet, we know there are limits to the body's natural ability to reverse damage to cells. We also know that there may be gaps in the ability of our genetic endowment to cope with damage. At some level, we all know it is just common sense to try to minimize damage to our bodies and maximize the ability to repair.

These opening paragraphs provide a quick introduction to the theme of this issue of Pathophysiology and a summary of the point of view of its authors. The public is currently interested in possible hazards from radio frequency (RF) due to cellphones, towers, WiFi, etc. The concern is certainly warranted, but we are surrounded by electromagnetic fields (EMFs) of many frequencies, and there are also significant biological effects and known risks from low frequency EMF. The scientific problem is to determine the nature of EMF interaction with biological systems and develop ways of coping with harmful effects in all frequency ranges, as well as their cumulative effects. The practical problem is to minimize the harmful biological effects of all EMF.

The technical papers in this issue are devoted to an examination and an evaluation of evidence gathered by scientists regarding the effects of EMF, especially RF radiation, on living cells and on the health of human populations. The laboratory studies point to significant interactions of both power frequency and RF with cellular components, especially DNA. The epidemiological studies point to increased risk of developing certain cancers associated with long-term exposure to RF. Overall, the scientific evidence shows that the risk to health is significant, and that to deny it is like being in free-fall and thinking 'so far, so good'. We must recognize that there is a potential health problem, and that we must begin to deal with it responsibly as individuals and as a society.

Table of contents

PathoPhysiology papers	Dates Received
EMF Effects on DNA	
Blank, Goodman	9/30
Phillips, Singh, Lai	10/14
Rudiger	12/22
EMF Effects on the Brain	
Nittby, Brun, Eberhardt, Malmgren, Persson, Salford	12/17
Hardell, Carlberg, Mild	10/16
Kundi, Hutter	9/1
Morgan	11/21
EMF in the Environment	
Davanipour, Sobel	11/1
Johansson	8/23
Pourlis	8/24
Balmori	7/21
Hutunnen, Hänninen, Myllylä	1/4
Blackman	11/13
Science as a Guide to Public Policy	
Gee	12/17
Sage, Carpenter	11/13

EMF effects on DNA

M. Blank and R. Goodman (USA): Electromagnetic Fields Stress Living Cells

Abbreviations: EMF, electromagnetic fields; Hz, hertz (cycles/s the unit of frequency); ELF, extremely low frequency ($3–3 \times 10^3$ Hz) power frequency is 50–60 Hz; RF, radio frequency (band width 3×10^3 to 3×10^{11} Hz); UHF, ultrahigh frequency band the RF sub-division used for cell phones (3×10^8 to 3×10^9 Hz).

0928-4680/$ – see front matter © 2009 Published by Elsevier Ireland Ltd.
doi:10.1016/j.pathophys.2009.02.002

J.L. Phillips, N.P. Singh and H. Lai (USA): Electromagnetic Fields and DNA damage

H.W. Rűdiger (Austria): Genotoxic effects of electromagnetic exposure in vitro

EMF effects on the brain

H. Nittby, A. Brun, J. Eberhardt, L. Malmgren, B.R.R. Persson and L.G. Salford (Sweden): Increased blood–brain barrier permeability in mammalian brain seven days after exposure to the radiation from a GSM-900 mobile phone

L. Hardell, M. Carlberg and K Hansson Mild (Sweden): Epidemiological evidence for an association between use of wireless phones and tumor diseases

M. Kundi and H-P. Hutter (Austria): Mobile phone base stations – effects on wellbeing and health

L.L. Morgan: Estimating the risk of brain tumors from cellphone use: published case–control studies

EMF in the environment

Z. Davanipour and E. Sobel: Long-term exposure to electromagnetic fields and the Risks of Alzheimer's disease and breast cancer: Further biological research

O. Johansson: Disturbance of the immune system by electromagnetic fields: A potentially underlying cause for cellular damage and tissue repair reduction which could lead to disease and impairment disturbance

A.F. Pourlis: Reproductive and developmental effects of EMF in vertebrate animal models

A. Balmori: Electromagnetic pollution from phone masts: Effects on wildlife

P. Huttunen, O. Hänninen and R.Myllylä: FM-radio and TV tower signals can cause spontaneous hand movements near moving RF reflector

C. Blackman: Cell Phone Radiation: Evidence from ELF and RF studies supporting more inclusive risk identification and assessment

Science as a guide to public policy

D. Gee: Late Lessons from early warnings: Towards realism and precaution with EMF?

C. Sage and D.O. Carpenter: Public Health Implications of Wireless Technologies

Special Issue on EMF

Bioelectromagnetics, the study of biological effects of electromagnetic fields (EMF), is an interdisciplinary science with a technical literature that is not easily accessible to the non-specialist. To increase access of the public to the technical literature and to the health implications of the scientific findings, the Bioinitiative Report was organized by an international group of scientists and published online at www.bioinitiative.org on August 31, 2007. The report has been widely read, and was cited in September 2008 by the European Parliament when it voted overwhelmingly that the current EMF safety standards were obsolete and needed to be reviewed.

This special issue of Pathophysiology includes scientific papers on the EMF issue by contributors to the Bioiniative Report, as well as others, and is prepared for scientists who are not specialists in bioelectromagnetics. Each paper is independent and self-contained. To help the reader appreciate how the different subjects contribute to an understanding of the EMF issue, the papers are arranged in groups that emphasize key areas, and the role of science in analyzing the problem and evaluating possible solutions. The subject headings are:

- DNA to show biological effects at the sub-cellular level that occur at very low EMF thresholds and across frequency ranges of the EM spectrum. Interactions with DNA may account for many of the effects of EMF, and they raise the possibility that genetic damage due to EMF can lead to cancer.
- The Brain is exposed to radiation from mobile phone antennas, and laboratory studies show that the radiation causes leakage of the protective blood–brain barrier, as well as the death of neurons in the brain. Radiation emitted from base stations can affect all who are in the vicinity. Epidemiological studies have shown a relation between exposure to mobile phones, base-stations and the development of brain tumors. Some epidemiological studies have significant flaws in design, and the risk of brain cancer may be greater than reported in the published results.
- In addition to the risk of brain cancer, EMF in the environment may contribute to diseases like Alzheimer's dementia and breast cancer in humans, as well as reproductive and developmental effects in animals in the wild. EMF affect the biochemical pathways and immunological mechanisms that link the different organ systems in our bodies and those of animals. The human body can act as an antenna for RF signals, and a small percentage of the population appears to be so sensitive to EMF that it interferes with their daily lives. In addition to the growing presence of EMF signals in the environment, the complexity of the signals may be important in altering biological responses. These are among the many factors that must be considered in approaching EMF safety issues.
- Science as a guide to public policy

Four centuries ago, when Francis Bacon envisioned a course for modern science, he expressed the idea that *knowledge is power that should be applied for the benefit of mankind.* It is in keeping with that ethical standard that the final papers in this issue show how knowledge gained from scientific research can help solve problems arising from EMF in our environment. The first of these papers discusses the Precautionary Principle, its growing acceptance as a rational approach to environmental issues, and how past experience can help us deal with the EMF issue. The second paper, by the editors of the original BioInitiative Report, is an update on how best to deal with the challenge of EMF in the environment and, specifically, the problems accompanying wireless technologies. The last paper describes the most recent in a

series of petitions by scientists demanding that society use our knowledge to deal effectively with the EMF issue.

We trust that the reviews and original research papers will increase awareness of the growing impact of EMF in the environment, and the need for modern society to deal expeditiously with the potential health problems brought to light by EMF research.

Guest Editor
Martin Blank
Physiology and Cellular Biophysics, Columbia University, New York, USA
E-mail address: mb32@columbia.edu

22 January 2009

ELSEVIER

Pathophysiology 16 (2009) 71–78

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Electromagnetic fields stress living cells

Martin Blank [a,*], Reba Goodman [b]

[a] *Department of Physiology, Columbia University, New York, NY, USA*
[b] *Department of Pathology, Columbia University, New York, NY, USA*

Received 30 January 2009; accepted 30 January 2009

Abstract

Electromagnetic fields (EMF), in both ELF (extremely low frequency) and radio frequency (RF) ranges, activate the cellular stress response, a protective mechanism that induces the expression of stress response genes, e.g., HSP70, and increased levels of stress proteins, e.g., hsp70. The 20 different stress protein families are evolutionarily conserved and act as 'chaperones' in the cell when they 'help' repair and refold damaged proteins and transport them across cell membranes. Induction of the stress response involves activation of DNA, and despite the large difference in energy between ELF and RF, the same cellular pathways respond in both frequency ranges. Specific DNA sequences on the promoter of the HSP70 stress gene are responsive to EMF, and studies with model biochemical systems suggest that EMF could interact directly with electrons in DNA. While low energy EMF interacts with DNA to induce the stress response, increasing EMF energy in the RF range can lead to breaks in DNA strands. It is clear that in order to protect living cells, EMF safety limits must be changed from the current thermal standard, based on energy, to one based on biological responses that occur long before the threshold for thermal changes.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: DNA; Biosynthesis; Electromagnetic fields; ELF; RF

1. Electromagnetic fields (EMF) alter protein synthesis

Until recently, genetic information stored in DNA was considered essentially invulnerable to change as it was passed on from parent to progeny. Mutations, such as those caused by cosmic radiation at the most energetic end of the EM spectrum, were thought to be relatively infrequent. The model of gene regulation was believed to be that the negatively charged DNA was tightly wrapped up in the nucleus with positively charged histones, and that most genes were 'turned off' most of the time. Of course, different regions of the DNA code are being read more or less all the time to replenish essential proteins that have broken down and those needed during cell division.

New insights into the structure and function of DNA have resulted from numerous, well-done laboratory studies. The demonstration that EMF induces gene expression and the synthesis of specific proteins [1,2] generated considerable controversy from power companies, government agencies, physicists, and most recently, cell phone companies. Physicists have insisted that the reported results were not possible because there was not enough energy in the power frequency range (ELF) to activate DNA. They were thinking solely of mechanical interaction with a large molecule and not of the large hydration energy tied up in protein and DNA structures that could be released by small changes in charge [3]. Of the biologists who accepted such results [4], most thought that the EMF interaction originated at, and was amplified by, the cell membrane and not with DNA.

It is now generally accepted that weak EMF in the power frequency range can activate DNA to synthesize proteins. An EMF reactive sequence in the DNA has been identified [5] and shown to be transferable to other gene promoters [6]. This DNA sequence acts as an EMF sensitive antenna

Abbreviations: EMF, electromagnetic fields; Hz, hertz; ELF, extremely low frequency; RF, radio frequency; MAPK, mitogen activated protein kinase; ERK1\2, extracellular signal regulated kinase; JNK, c-Jun-terminal kinase p38MAPK; SAPK, stress activated protein kinase; NADH, nicotinamide adenine dinucleotide dehydrogenase; ROS, reactive oxygen species.

* Corresponding author at: Department of Physiology, Columbia University, 630 West 168 Street, New York, NY 10032, USA. Tel.: +1 212 305 3644; fax: +1 212 305 5775.
E-mail address: mb32@columbia.edu (M. Blank).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.006

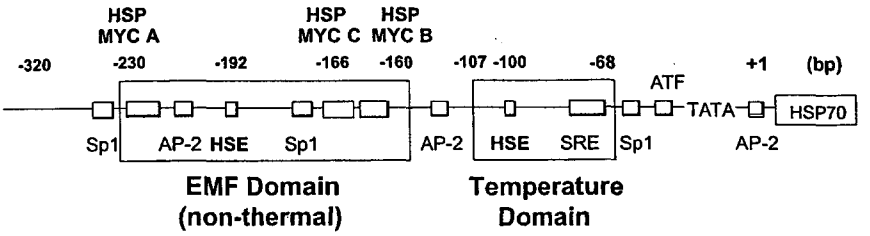


Fig. 1. Diagram of the HSP70 promoter showing the two different DNA sequences that have been identified as activated by EMF (non-thermal) and by thermal stimuli, respectively. The EMF domain contains three nCTCTn consensus sequences (electromagnetic response elements; EMRE), and differs from the consensus sequence (nGAAn) in the temperature or thermal domain.

that responds to EMF when transfected into reporter genes. Research at the more energetic levels of power frequency [7] and in the RF [8] ranges has shown that exposure to EMF can lead to breaks in the DNA strands. Therefore, DNA can no longer be considered unaffected by environmental EMF levels. It can be activated and damaged by EMF at levels that are considered safe [9]. The vulnerability of DNA to environmental influences and the possible dangers associated with EMF, had been underscored by discovery of EMF activation of the cellular stress response in the ELF range [10,11]. The cellular stress response is an unambiguous signal by the cell that EMF is potentially harmful.

2. Physiological stress and cellular stress

Discussions of physiological stress mechanisms usually describe responses of the body to pain, fear, 'oxygen debt' from muscle overexertion. These responses are mediated by organ systems. For example, the nervous system transmits action potentials along a network of nerves to cells, such as adrenal glands, that release rapidly acting agents such as epinephrine and norepinephrine and slower acting mineralocorticoids. These hormones are transported throughout the body by the circulatory system. They mobilize the defenses to cope with the adverse conditions and enable the body to 'fight or flee' from the noxious stimuli. The defensive actions include changes in heart rate, breathing rate, muscle activity, etc.

In addition to the responses of organ systems, there are protective mechanisms at the cellular level known as the cellular stress response. These mechanisms are activated by damage to cellular components such as DNA and protein [12], and the responses are characterized by increased levels of stress proteins [13] indicating that stress response genes have been upregulated in response to the stress.

The first stress response mechanism identified was the cellular reaction to sharp increases in temperature [14] and was referred to as 'heat shock', a term that is still retained in the nomenclature of the protective proteins, the hsps, heat shock proteins. Stress proteins are designated by the prefix 'hsp' followed by a number that gives the molecular weight in kilodaltons. There are about 20 different protein families ranging in molecular weight from a few kilodaltons to over 100 kD, with major groups of proteins around 30 kD, 70 kD and 90 kD.

Research on the 'heat shock' response has shown that hsp synthesis is activated by a variety of stresses that are potentially harmful to cells, including physical stimuli like pH and osmotic pressure changes, as well as chemicals such as alcohol and toxic metal ions like Cd^{2+}. EMF is a recent addition to the list of physical stimuli. It was initially shown in the power frequency (extremely low frequency, ELF) range [13], but shortly afterwards, radio frequency (RF) fields [15] and amplitude modulated RF fields [16] were shown to activate the same stress response.

Studies of stress protein stimulation by low frequency EMF have focused on a specific DNA sequence in the gene promoter that codes for hsp70, a major stress protein. Synthesis of this stress protein is initiated in a region of the promoter (see Fig. 1) where a transcription factor known as heat shock factor 1 (HSF-1) binds to a heat shock element (HSE). This EMF sensitive region on the HSP70 promoter is upstream from the thermal domain of the promoter and is not sensitive to increased temperature. The binding of HSF-1 to HSE occurs at −192 in the HSP70 promoter relative to the transcription initiation site. The EMF domain contains three nCTCTn myc-binding sites −230, −166 and −160 relative to the transcription initiation site and upstream of the binding sites for the heat shock (nGAAn) and serum responsive elements [5,6,17,18]. The electromagnetic response elements (EMREs) have also been identified on the c-*myc* promoter and are also responsive to EMF. The sensitivity of the DNA sequences, nCTCTn, to EMF exposures has been demonstrated by transfecting these sequences into CAT and Luciferase reporter genes [6]. Thus, the HSP70 promoter contains different DNA regions that are specifically sensitive to different stressors, thermal and non-thermal.

Induction of increased levels of the major stress protein, hsp70, by EMF is rapid, within 5 min. Also it occurs at extremely low levels of energy input, 14 orders of magnitude lower than with a thermal stimulus [10]. The far greater sensitivity to EMF than to temperature change in elevating the protective protein, hsp70, has been demonstrated to have potential clinical application, preventing injury from ischemia reperfusion [19–21]. George et al. [22] have shown the non-invasive use of EMF-induced stress proteins improved hemodynamic parameters during reperfusion

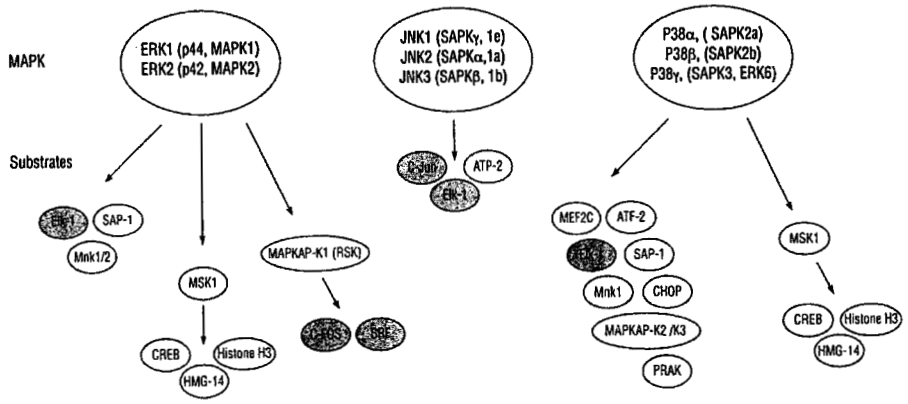


Fig. 2. The four mitogen activated protein kinase (MAPK) signaling cascades identified to date are: extracellular signal regulated kinase 1/2 (ERK), c-Jun-terminal kinase (JNK), p38MAPK and stress activated protein kinase (SAPK). Elements of the three MAPkinase pathways that have been identified as activated by EMF are shown as the shaded circles.

following ischemia. This effect occurred in the absence of measurable increased temperature.

3. EMF interaction with signaling pathways

EMF penetrate cells unattenuated and so can interact directly with the DNA in the cell nucleus, as well as other cell constituents. However, biological agents are impeded by membranes and require special mechanisms to gain access to the cell interior. Friedman et al. [23] have demonstrated that the initial step in transmitting extracellular information from the plasma membrane to the nucleus of the cell occurs when NADH oxidase rapidly generates reactive oxygen species (ROS). These ROS stimulate matrix metalloproteinases that allow them to cleave and release heparin binding epidermal growth factor. This secreted factor activates the epidermal growth receptor, which in turn activates the extracellular signal regulated kinase 1\2 (ERK) cascade. The ERK cascade is one of the four mitogen-activated protein kinase (MAPK) signaling cascades that regulate transcriptional activity in response to extracellular stimuli. The elements of the three MAPK signaling cascades implicated in exposures to ELF and RF are highlighted in Fig. 2.

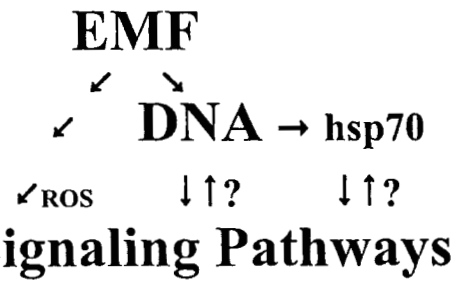


Fig. 3. The signaling pathways and the stress response are activated by EMF. The activation mechanisms discussed in the text are indicated by arrows. In the stress response, DNA activation leads to hsp synthesis and may be due to direct EMF interaction with DNA. The signaling pathways are activated by reactive oxygen species (ROS) that are probably generated by EMF. Possible interactions between the pathways, DNA and hsp are indicated with question marks. In any case, EMF leads to activation of all the processes shown.

The four MAPK cascades are: (1) ERK, (2) c-Jun-terminal kinase (JNK), (3) stress activated protein kinase (SAPK) and (4) p38SAPK. Each of the cascades is composed of three to six tiers of protein kinases, and their signals are transmitted by sequential phosphorylation and activation of the protein kinases in each of the tiers. The result is activation of a large number of regulatory proteins, which include a set of transcription factors, e.g., c-Jun, c-Fos, hsp27 and hsp70. Activation of the stress response is accompanied by activation of specific signal transduction cascades involved in regulating cell proliferation, differentiation and metabolism [24–26]. The MAPK pathways have been characterized in several cell types [24,27–30]. Exposure to non-thermal ELF as well as thermal RF affects the expression of many cellular proteins [23–25] (Fig. 3).

The elevated expression of these protein transcription factors participate in the induction of various cellular processes, including several that are affected by cell phones, e.g., replication and cell-cycle progression [25,31] and apoptosis [32]. RF fields have been shown to activate specific transcription factor binding that stimulate cell proliferation and induce stress proteins [25,33]. It has been reported [31] that within 10 min of cell phone exposures, two MAPKinase cascades, p38 and ERK1\2, are activated. Both ELF and RF activate the upregulation of the HSP70 gene and induction of elevated levels of the hsp70 protein. This effect on RNA transcription and protein stability is controlled by specific protein transcription factors that are elements of the mitogen MAPK cascade.

EMF also stimulate serum response factor which binds to the serum response element (SRE) through ERK MAPK activation and is associated with injury and repair *in vivo* and *in vitro*. The SRE site is on the promoter of an early response gene, c-fos, which under specific cellular circumstances has oncogenic properties. The c-fos promoter is EMF-sensitive; a 20 min exposure to 60 Hz 80mG fields significantly increases c-*fos* gene expression [34]. The SRE accessory protein,

Elk-1, contains a growth-regulated transcriptional activation domain. ERK phosphorylation potentiates Elk-1 and transactivation at the c-*fos* SRE [29].

During the past twenty years, the growing use of cellular phones has aroused great concern regarding the health effects of exposure of the brain to 900 MHz RF waves. Despite claims that the energy level is too low to induce changes in DNA and that the devices are safe, the non-thermal effects that have been demonstrated at both ELF and RF exposure levels can cause physiological changes in cells and tissues even at the level of DNA. Finally, it should be mentioned that some of the pathways described in this section also have roles in protein synthesis via RNA polymerase III, an enzyme in oncogenic pathways [35] and could, therefore, provide a mechanistic link between cancer and EMF exposure.

4. Cells affected by the stress response

Reviews on EMF and the stress response have appeared for the ELF range [13] and for the RF range [36]. The most recent review was published online in section 7 of the Bioinitiative Report [9], and it summarized both ELF and RF studies, mainly at frequencies 50 Hz, 60 Hz, 900 MHz and 1.8 GHz. The citations in that review were not exhaustive, but the different frequencies and biological systems represent the diversity of results on stimulation of DNA and stress protein synthesis in many different cells. It is clear that the stress response does not occur in reaction to EMF in all types of cells, and sometimes because of the use of tissue cultured cell lines, even the same cell line can give opposite results in the same laboratory [37].

Many different types of cells have been shown to respond to EMF, both *in vivo* and *in vitro*, including epithelial, endothelial and epidermal cells, cardiac muscle cells, fibroblasts, yeast, *E. coli*, developing chick eggs, and dipteran cells (see Bioinitiative Report [9], section 7). Tissue cultured cells are less likely to show an effect of EMF, probably because immortalized cells have been changed significantly to enable them to live indefinitely in unnatural laboratory conditions. This may also be true of cancer cells, although some (e.g., MCF7 breast cancer cells) have responded to EMF [38,39], and in HL60 cells, one cell line responds to EMF while another does not [24]. Czyz et al. [16] found that p53-deficient embryonic stem cells showed an increased EMF response, but the wild type did not.

A broad study of genotoxic effects (i.e., DNA damage) in different kinds of cells [40] found no effects with lymphocytes, monocytes and skeletal muscle cells, but did find effects with fibroblasts, melanocytes and rat granulosa cells. Other studies [41,42] have also found that the blood elements, such as lymphocytes and monocytes are natural cells that have not responded. Since mobile cells can easily move away from a stress, there would be little selective advantage and evolutionary pressure for developing the stress response. The lack of response by skeletal muscle cells is related to the need to desensitize the cells to excessive heating during activity. Unlike slow muscle fibers that do synthesize hsp70, cells containing fast muscle fibers do not synthesize hsp70 to protect them from over-reacting to the high temperatures reached a during activity.

Table 1
Biological thresholds in the ELF range.

Biological system	Threshold (μT)[a]	Reference
Acceleration of reaction rates		
Na,K-ATPase	0.2–0.3	Blank and Soo [49]
cytochrome oxidase	0.5–0.6	Blank and Soo [43]
ornithine decarboxylase	~2	Mullins et al. [58]
malonic acid oxidation	<0.5	Blank and Soo [59]
Biosynthesis of stress proteins		
HL60, Sciara, yeast,	<0.8	Goodman et al. [11]
breast (HTB124, MCF7)	<0.8	Lin et al. [39]
chick embryo (anoxia)	~2	DiCarlo et al. [60]
Breast cancer (MCF7) cell growth		
block melatonin inhibition	0.2 < 1.2	Liburdy et al. [38]
Leukemia epidemiology	0.3–4	Ahlbom et al. [61] Greenland et al. [62]

[a] 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.

5. EMF–DNA interaction mechanisms: electron transfer

The biochemical compounds in living cells are composed of charges and dipoles that can interact with electric and magnetic fields by various mechanisms. An example discussed earlier is the generation of reactive oxygen species (ROS) in activation of the ERK signaling cascade. The cellular stress response leading to the synthesis of stress proteins is also activated by EMF. However, the specific reaction is not known, except that it is stimulated by very weak EMF. For this reason, our focus has been on molecular processes that are most sensitive to EMF and that could cause the DNA to come apart to initiate biosynthesis. We have suggested that direct EMF interaction with electrons in DNA is likely for the following reasons:

- The largest effects of EMF would be expected on electrons because of their high charge to mass ratio. At the sub-atomic level, one assumes that electrons respond instantaneously compared to protons and heavier atomic nuclei, as in the Born-Oppenheimer Approximation. The very low field strengths and durations that activate the stress response and other reactions (Table 1) suggest interaction with electrons, and make ion-based mechanisms unlikely.
- Weak ELF fields have been shown to affect the rates of electron transfer reactions [43,44]. A 10 μT magnetic field exerts a very small force of only $\sim 10^{-20}$ N on a unit charge,

but this force can move an isolated electron more than a bond length, ~1 nm, in ~1 nanosecond.

- There is a specific EMF responsive DNA sequence that is associated with the response to EMF (Fig. 1), and that retains this property when transfected
- Displacement of electrons in DNA would cause local charging that has been shown to lead to disaggregation of biopolymers [45].
- As the energy in an EMF stimulus increases, there is an increase in single strand breaks, followed by double strand breaks, suggesting an interaction with EMF at all energy levels [46].

Effects of EMF on electrons in chemical reactions were detected indirectly in studies on the Na,K-ATPase [47], a ubiquitous enzyme that establishes the normal Na and K ion gradients across cell membranes. Electric and magnetic fields, each accelerated the reaction only when the enzyme was relatively inactive. It is reasonable to assume that the threshold response occurs when the same charge is affected by the two fields, so the velocity (v) of the charge (q) could be calculated from these measurements and its nature determined. Assuming both fields exert the same force at the threshold, the electric (E) and the magnetic (B) forces should be equal.

$$F = qE = qvB. \quad (1)$$

From this $v = E/B$, the ratio of the threshold fields, and by substituting the measured thresholds [48,49], $E = 5 \times 10^{-4}$ V/m and $B = 5 \times 10^{-7}$T (0.5 μT), we obtain $v = 10^3 m/s$. This very rapid velocity, similar to that of electrons in DNA [50], indicated that electrons were probably involved in the ion transport mechanism of the Na,K-ATPase [47]. An electron moving at a velocity of 10^3 m/s crosses the enzyme (~10^{-8} m) before the ELF field has had a chance to change. This means that a low frequency sine wave signal is effectively a repeated DC pulse. This is true of all low frequency effects on fast moving electrons.

Studies of effects of EMF on electron transfer in cytochrome oxidase, ATP hydrolysis by the Na,K-ATPase, and the Belousov–Zhabotinski (BZ) redox reaction, have led to certain generalizations:

- EMF can accelerate reaction rates, including electron transfer rates
- EMF acts as a force that competes with the chemical forces in a reaction. The effect of EMF varies inversely with the intrinsic reaction rate, so EMF effects are only seen when intrinsic rates are low. (This is in keeping with the therapeutic efficacy of EMF on injured tissue, while there is usually little or no effect on normal tissue.)
- Experimentally determined thresholds are low (~0.5 μT) and comparable to levels found by epidemiology. See Table 1.
- Effects vary with frequency, with different optima for the reactions studied: The two enzymes showed broad frequency optima close to the reaction turnover numbers for Na,K-ATPase (60 Hz) and cytochrome oxidase (800 Hz), suggesting that EMF interacted optimally when in synchrony with the molecular kinetics. This is not true for EMF interactions with DNA, which are stimulated in both ELF and RF ranges and do not appear to involve electron transfer reactions with well-defined kinetics.

Probably the most convincing evidence for a frequency sensitive mechanism that involves stimulation of DNA is activation of protein synthesis in striated muscle. In this natural process, specific muscle proteins are synthesized by varying the rate of the (electrical) action potentials in the attached nerves [51]. The ionic currents of the action potentials that flow along and through the muscle membranes, also pass through the muscle cell nuclei that contain the DNA codes for the muscle proteins. Two frequencies were studied in muscle, high (100 Hz) and low (10 Hz) frequency, corresponding to the frequencies of the fast muscles and slow muscles that have different contraction rates and different muscle proteins. In the experiments, either the fast or slow muscle proteins were synthesized at the high or low frequency stimulation rates corresponding to the frequency of the action potentials. The clear dependence of the protein composition on the frequency of the action potentials indicates a relation between stimulation and activation of DNA in muscle physiology. The process is undoubtedly far more complicated and unlikely to be a simple electron transfer reaction as with cytochrome oxidase. It is more probable that an entire region of DNA coding for a group of related proteins is activated simultaneously.

A mechanism based on electron movement is in keeping with the mV/m electric field and μT magnetic field thresholds that affect the Na,K-ATPase. The very small force on a charge (~10^{-20} N) can affect an electron, but is unlikely to have a direct effect on much more massive ions and molecules, especially if they are hydrated. Ions are affected by the much larger DC electric fields of physiological membrane processes. The low EMF energy can move electrons, cause small changes in charge distribution and release the large hydration energy tied up in protein and DNA structures [3]. Electrons have been shown to move in DNA at great speed [50], and we have suggested that RF and ELF fields initiate the stress response by directly interacting and accelerating electrons moving within DNA [52,53].

A mechanism based on electron movement also provides insight into why the same stress response is stimulated by both ELF and RF even though the energies of the two stimuli differ by orders of magnitude. A typical ELF cycle at 10^2Hz lasts 10^{-2} s and a typical RF cycle at 10^{11} Hz lasts 10^{-11} s. Because the energy is spread over a different number of cycles/second in the two ranges, the energy/cycle is the same in both ELF and RF ranges. Since electron movement occurs much faster than the change of field, both frequencies are seen by rapidly moving electrons as essentially DC pulses. Each cycle contributes to electron movement at both

frequencies, but more rapidly at the higher frequency. The fluctuation of protons between water molecules in solution at a frequency of about 10^{12} Hz [54] gives an indication of the speed of electron movement, and may suggest an upper limit of the frequency in which sine wave EMF act as DC pulses.

6. DNA biology and the EM spectrum

Research on DNA and the stress response has shown that the same biology occurs across divisions of the EM spectrum, and that EMF safety standards based on cellular measures of potential harm should be much stricter. These data also raise questions about the utility of spectrum sub-divisions as the basis for properly assessing biological effects and setting separate safety standards for the different sub-divisions. The frequencies of the EM spectrum form a continuum, and division into frequency bands is only a convenience that makes it easier to assign and regulate different portions of the spectrum for practical uses, such as the different design requirements of devices for EMF generation and measurement. Except for the special case of the visual range, the frequency bands are not based on biology, and the separate bands now appear to be a poor way of dealing with biological responses needed for evaluating safety. The DNA studies indicate the need for an EMF safety standard rooted in biology and a rational basis for assessing health implications.

DNA responses to EMF can be used to create a single scale for evaluation of EMF dose because:

- The same biological responses are stimulated in ELF and RF ranges.
- The intensity of EMF interactions with DNA leads to greater effects on DNA as the energy increases with frequency. In the ELF range, the DNA is only activated to initiate protein synthesis, while single and double strand breaks occur in the more energetic RF and ionizing ranges.

A scale based on DNA biology also makes possible an approach to a quantitative relation between EMF dose and disease. This can be done by utilizing the data banks that have been kept for A-bomb exposure and victims of nuclear accidents, data that link exposure to ionizing radiation and subsequent development of cancer. Utilizing experimental studies of DNA breaks with ionizing radiation, it is possible in principle to relate cancer incidence to EMF exposures. It should be possible to determine single and double strand breaks in a standard preparation of DNA, caused by exposure to EMF for a specified duration, under standard conditions. Although many studies of DNA damage and repair rates under different conditions would be needed, this appears to be a possible experimental approach to assessing the relation between EMF exposure and disease.

7. The stress response and safety standards

Most scientists believe that basic research eventually pays off in practical ways. This has certainly been true of EMF research on the stress response, where EMF stimulated stress proteins have been used to minimize damage to ischemic tissues on reperfusion. However, more importantly, biological effects stimulated by both ELF and RF have shown that the standards used for developing safety guidelines are not protective of cells.

First and foremost, it is important to realize that the stress response occurs in reaction to a potentially harmful environmental influence. The stress response is an unambiguous indication that cells react to EMF as potentially harmful. It is therefore an indication of compromised cell safety, given by the cell, in the language of the cell. The low threshold level of the stress response shows that the current safety standards are much too high to be considered safe.

In general, cellular processes are unusually sensitive to fields in the environment. The biological thresholds in the ELF range (Table 1) are in the range of 0.5–1.0 μT—not very much higher than the ELF backgrounds of ~0.1 μT. The relatively low field strengths that can affect biochemical reactions is a further indication that cells are able to sense potential danger long before there is an increase in temperature.

EMF research has also shown that exposure durations do not have to be prolonged to have an effect. Litovitz et al. [55,56], working with the enzyme ornithine decarboxylase, showed an EMF response when cells were exposed for only 10 s to ELF or ELF modulated 915 MHz, providing that the exposure was continuous. Gaps in the sine wave resulted in a reduced response, and interference with the sine wave in the form of superimposed ELF noise also reduced the response [57]. The interfering effect of noise has been shown in the RF range by Lai and Singh [46], who reported that noise interferes with the ability of an RF signal to cause breaks in DNA strands. The decreased effect when noise is added to a signal is yet another indication that EMF energy is not the critical factor in causing a response. In fact, EMF noise appears to offer a technology for mitigating potentially harmful effects of EMF in the environment.

EMF research has shown that the thermal standard used by agencies to measure safety is at best incomplete, and in reality not protective of potentially harmful non-thermal fields. Non-thermal ELF mechanisms are as effective as thermal RF mechanisms in stimulating the stress response and other protective mechanisms. The current safety standard based on thermal response is fundamentally flawed, and not protective.

Finally, since both ELF and RF activate the same biology, simultaneous exposure to both is probably additive and total EMF exposure is important. Safety standards must consider total EMF exposure and not separate standards for ELF and RF ranges.

References

[1] R. Goodman, C.A.L. Bassett, A. Henderson, Pulsing electromagnetic fields induce cellular transcription, Science 220 (1983) 1283–1285.

[2] R. Goodman, A. Henderson, Exposure of salivary gland cells to low frequency electromagnetic fields alters polypeptide synthesis, PNAS 85 (1988) 3928–3932.

[3] M. Blank, Protein and DNA interactions with electromagnetic fields, Electromagn Biol Med 28 (2008) 3–23.

[4] W.R. Adey, Tissue interactions with non-ionizing electromagnetic fields, Physiol Rev 61 (1981) 435–514.

[5] H. Lin, M. Blank, R. Goodman, A magnetic field responsive domain in the human HSP70 promoter, J Cell Biochem 75 (1999) 170–176.

[6] H. Lin, M. Blank, K. Rossol-Haseroth, R. Goodman, Regulating genes with electromagnetic response elements, J Cell Biochem 81 (2001) 143–148.

[7] REFLEX Project Report, 2004, A summary of the final report can be found at http://www.verum-foundation.de/www2004/html/pdf/euprojekte01/REFLEX_ProgressSummary_231104.pdf.

[8] H. Lai, N.P. Singh, Acute exposure to a 60 Hz magnetic field increases DNA strand breaks in rat brain cells, Bioelectromagnetics 18 (1997) 156–165.

[9] Bioinitiative Report, edited by C. Sage, D. Carpenter, A Scientific Perspective on Health Risk of Electromagnetic Fields, published online 31 August 2007 http://www.bioinitiative.org/report/index.htm.

[10] M. Blank, O. Khorkova, R. Goodman, Changes in polypeptide distribution stimulated by different levels of EM and thermal stress, Bioelectrochem Bioenerg 33 (1994) 109–114.

[11] R. Goodman, M. Blank, H. Lin, O. Khorkova, L. Soo, D. Weisbrot, A.S. Henderson, Increased levels of hsp70 transcripts are induced when cells are exposed to low frequency electromagnetic fields, Bioelectrochem Bioenerg 33 (1994) 115–120.

[12] D. Kultz, Molecular, Evolutionary basis of the cellular stress response, Ann Rev Physiol 67 (2005) 225–257.

[13] R. Goodman, M. Blank, Magnetic field stress induces expression of hsp70, Cell Stress Chaperones 3 (1998) 79–88.

[14] F.M. Ritossa, A new puffing pattern induced by a temperature shock and DNP in *Drosophila*, Experientia Basel 18 (1962) 571–573.

[15] D.I. de Pomerai, C. Daniells, H. David, J. Allan, I. Duce, M. Mutwakil, D. Thomas, P. Sewell, J. Tattersall, D. Jones, Non-thermal heat-shock response to microwaves, Nature 6785 (2000) 417–418.

[16] J. Czyz, K. Guan, Q. Zeng, T. Nikolova, A. Meister, F. Schönborn, I. Schuderer, N. Kuster, A.M. Wobus, High frequency electromagnetic fields (GSM signals) affect gene expression levels in tumor suppressor p53-deficient embryonic stem cells, Bioelectromagnetics 25 (2004) 296–307.

[17] T. Taira, Y. Negishi, F. Kihara, S.M.M. Iguchi-Ariga, H. Ariga, H. c-myc protein complex binds to two sites in human hsp70 promoter region, Biochim Biophys Acta 1130 (1992) 166–174.

[18] J. Topol, D.M. Ruden, C.S. Parker, Sequences required for in vitro transcriptional activation of a drosophila hsp70 gene, Cell 42 (1985) 527–537.

[19] A. Albertini, B. Zucchini, G. Noera, R. Cadossi, C.P. Napoleone, A. Pierangeli, Protective effect of low frequency low energy policy electromagnetic fields on acute experimental myocardial infarcts in rats, Bioelectromagnetics 20 (1999) 372–377.

[20] A. Di Carlo, J.M. Farrell, T. Litovitz, A simple experiment to study electromagnetic field effects: protection induced by short-term exposures to 60 Hz magnetic fields, Bioelectromagnetics 19 (1998) 498–500.

[21] J.M. Shallom, A.L. DiCarlo, D. Ko, L.M. Penafiel, A. Nakai, Microwave exposure induces hsp70 and confers protection against hypoxia in chick embryos, J Cell Biochem 86 (2002) 490–496.

[22] I. George, M. Geddis, Z. Lill, H. Lin, T. Gomez, M. Blank, M. Oz, R. Goodman, Myocardial function improved by electromagnetic fields induction of stress protein hsp70, J Cellular Physiol 216 (2008) 816–823, published online: doi:10.1002/jcp.21461.

[23] J. Friedman, S. Kraus, Y. Hauptman, Y. Schiff, R. Seger, Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies, Biochem J 405 (2007) 559–568.

[24] M. Jin, M. Blank, R. Goodman, ERK1/2 phosphorylation, induced by electromagnetic fields, diminishes during neoplastic transformation, J Cell Biochem 78 (2000) 371–379.

[25] D. Leszczynski, S. Joenvaara, J. Reivinen, R. Kuokka, Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: molecular mechanism for cancer-and blood-brain barrier-related effects, Differentiation 70 (2002) 120–129.

[26] M. Simko, Induction of cell activation processes by low frequency electromagnetic fields, ScientificWorldJournal 4 (Suppl. 2) (2004) 4–22.

[27] R. Marais, J. Wynne, R. Treisman, The SRF accessory protein Elk-1 contains a growth factor-regulated transcriptional activation domain, Cell 73 (1993) 381–393.

[28] R. Janecht, W.H. Ernst, V. Pigoud, A. Nordheim, Activation of TCF Elk-1 by MAP kinases, EMBO J 12 (1993) 5097–5104.

[29] H. Gille, M. Kortenjann, O. Thomae, C. Moomaw, C. Slaughter, M.H. Cobb, P.E. Shaw, ERK phosphorylation potentiates Elk-1-mediated ternary complex formation and transactivation, EMBO J 14 (1995) 951–962.

[30] V. Sgambato, P. Vanhouttte, C. Pages, M. Rogard, L. Hipskind, M.J. Besson, J. Caboche, In vivo expression and regulation of Elk-1, a target of the extracellular-regulated kinase signaling pathway, in the rat brain, J. Neurosci 18 (1998) 214–226.

[31] D. Leszczynski, R. Nylund, S. Joevaara, J. Reivinen, Applicability of discovery science approach to determine biological effects of mobile phone radiation, Proteonomics 4 (2004) 426–431.

[32] G.J. Hook, P. Zhang, I. Lagroye, L.E. Li, R. Higashikubo, E.G. Moros, W.L. Starube, W.F. Pickard, J.D. Baty, J.L. Roti-Roti, Measurement of DNA damage and apoptosis in Molt-4 cells after in vitro exposure to radio frequency radiation, Radiat Res 161 (2004) 193–200.

[33] D. Weisbrot, H. Lin, L. Ye, M. Blank, R. Goodman, Effects of mobile phone radiation on growth and development in *Drosophila melanogaster*, J Cell Biochem 89 (2003) 48–55.

[34] S. Rao, A.S. Henderson, Regulation of c-fos is affected by electromagnetic fields, J Cell Biochem 63 (1996) 358–365.

[35] D.L. Johnson, S.A.S. Johnson, RNA metabolism and oncogenesis, Science 320 (2008) 461–462.

[36] I.A. Cotgreave, Biological stress responses to radio frequency electromagnetic radiation: are mobile phones really so (heat) shocking? Arch Biochem Biophys 435 (2005) 227–240.

[37] M. Jin, H. Lin, L. Han, M. Opler, S. Maurer, M. Blank, R. Goodman, Biological and technical variables in myc expression in HL60 cells exposed to 60 Hz electromagnetic fields, Bioelectrochem Bioenerg 44 (1997) 111–120.

[38] R.P. Liburdy, T.R. Sloma, R. Sokolic, P. Yaswen, ELF magnetic fieklds, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER+ breast cancer cell proliferation, J Pineal Res 14 (1993) 89–97.

[39] H. Lin, M. Head, M. Blank, L. Han, M. Jin, R. Goodman, Myc-mediated transactivation of HSP70 expression following exposure to magnetic fields, J Cell Biochem 69 (1998) 181–188.

[40] S. Ivancsits, A. Pilger, F. Diem, O. Jahn, H. Rudiger, Cell type-specific genotoxic effects of intermittent extremely low-frequency electromagnetic fields, Mutation Res 583 (2005) 184–188.

[41] M. Lantow, M. Lupke, J. Frahm, M.O. Mattsson, N. Kuster, M. Simko, ROS release and Hsp70 expression after exposure to 1,800 MHz radiofrequency electromagnetic fields in primary human monocytes and lymphocytes, Radiat Environ Biophys 45 (2006) 55–62.

[42] M. Simko, C. Hartwig, M. Lantow, M. Lupke, M.O. Mattsson, Q. Rahman, J. Rollwitz, Hsp70 expression and free radical release after exposure to non-thermal radio-frequency electromagnetic fields and ultrafine particles in human Mono Mac 6 cells, Toxicol Lett 161 (2006) 73–82.

[43] M. Blank, L. Soo, Enhancement of cytochrome oxidase activity in 60 Hz magnetic fields, Bioelectrochem Bioenerg 45 (1998) 253–259.
[44] M. Blank, L. Soo, Electromagnetic acceleration of the Belousov-Zhabotinski reaction, Bioelectrochem 61 (2003) 93–97.
[45] M. Blank, L. Soo, Surface free energy as the potential in oligomeric equilibria: prediction of hemoglobin disaggregation constant, Bioelectrochem Bioenerg 17 (1987) 349–360.
[46] H. Lai, N.P. Singh, Interaction of microwaves and a temporally incoherent magnetic field on single and double DNA strand breaks in rat brain cells, Electromagn Biol Med 24 (2005) 23–29.
[47] M. Blank, A proposed explanation for effects of electric and magnetic fields on the Na,K-ATPase in terms of interactions with electrons, Bioelectromagnetics 26 (2005) 591–597.
[48] M. Blank, L. Soo, The threshold for alternating current inhibition of the Na,K-ATPase, Bioelectromagnetics 13 (1992) 329–333.
[49] M. Blank, L. Soo, The threshold for Na,K-ATPase stimulation by electromagnetic fields, Bioelectrochem Bioenerg 40 (1996) 63–65.
[50] C. Wan, T. Fiebig, S.O. Kelley, C.R. Treadway, J.K. Barton, Femtosecond dynamics of DNA-mediated electron transfer, Proc Nat Acad Sci U S A 96 (1999) 6014–6019.
[51] M. Blank, Electric stimulation of protein synthesis in muscle, Adv Chem 250 (1995) 143–153.
[52] M. Blank, R. Goodman, Initial interactions in electromagnetic field-induced biosynthesis, J Cell Physiol 199 (2004) 359–363.
[53] M. Blank, R. Goodman, A mechanism for stimulation of biosynthesis by electromagnetic fields: charge transfer in DNA and base pair separation, J Cell Physiol 214 (2008) 20–26.
[54] C.J. Fecko, J.D. Eaves, J.J. Loparo, A. Tokmakoff, P.L. Geissler, Ultrafast hydrogen-bond dynamics in infrared spectroscopy of water, Science 301 (2003) 1698–1701.
[55] T.A. Litovitz, D. Kraus, J.M. Mullins, Effect of coherence time of the applied magnetic field on ornithine decarboxylase activity, Biochem Biophys Res Comm 178 (1991) 862–865.
[56] T.A. Litovitz, D. Kraus, M. Penafiel, E.C. Elson, J.M. Mullins, The role of coherence time in the effect of microwaves on ornithine decarboxylase activity, Bioelectromagnetics 14 (1993) 395–403.
[57] J.M. Mullins, T.A. Litovitz, M. Penafiel, A. Desta, A. Krause, Intermittent noise affects EMF- induced ODC activity, Bioelectrochem Bioenerg 44 (1998) 237–242.
[58] J.M. Mullins, L.M. Penafiel, J. Juutilainen, T.A. Litovitz, Dose-response of electromagnetic field-induced ornithine decarboxylase activity, Bioelectrochem Bioenerg 48 (1999) 193–199.
[59] M. Blank, L. Soo, Electromagnetic acceleration of electron transfer reactions, J Cell Biochem 81 (2001) 278–283.
[60] A.L. Di Carlo, J.M. Mullins, T.A. Litovitz, Thresholds for EM field-induced hypoxia protection: evidence for a primary, electric field effect, Bioelectrochem 52 (2000) 9–16.
[61] H. Ahlbom, N. Day, M. Feychting, E. Roman, J. Skinner, J. Dockerty, M. Linet, M. McBride, J. Michaelis, J.H. Olsen, T. Tynes, P.K. Verkasalo, A pooled analysis of magneticfields and childhood leukemia, Brit J Cancer 83 (2000) 692–698.
[62] S. Greenland, A.R. Sheppard, W.T. Kaune, C. Poole, M.A.A. Kelsh, Pooled Analysis of Magnetic Fields, Wire Codes, and Childhood Leukemia, Epidemiology 11 (2000) 624–634.

ELSEVIER

Pathophysiology 16 (2009) 79–88

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Electromagnetic fields and DNA damage

J.L. Phillips [a,*], N.P. Singh [b], H. Lai [b]

[a] *Department of Chemistry, University of Colorado at Colorado Springs, Colorado Springs, CO 80918, USA*
[b] *Department of Bioengineering, University of Washington, Seattle, WA 98195, USA*

Received 24 October 2008; received in revised form 16 November 2008; accepted 16 November 2008

Abstract

A major concern of the adverse effects of exposure to non-ionizing electromagnetic field (EMF) is cancer induction. Since the majority of cancers are initiated by damage to a cell's genome, studies have been carried out to investigate the effects of electromagnetic fields on DNA and chromosomal structure. Additionally, DNA damage can lead to changes in cellular functions and cell death. Single cell gel electrophoresis, also known as the 'comet assay', has been widely used in EMF research to determine DNA damage, reflected as single-strand breaks, double-strand breaks, and crosslinks. Studies have also been carried out to investigate chromosomal conformational changes and micronucleus formation in cells after exposure to EMF. This review describes the comet assay and its utility to qualitatively and quantitatively assess DNA damage, reviews studies that have investigated DNA strand breaks and other changes in DNA structure, and then discusses important lessons learned from our work in this area.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Electromagnetic field; DNA damage; Comet assay; Radiofrequency radiation; Cellular telephone

1. The comet assay for measurement of DNA strand breaks

DNA is continuously damaged by endogenous and exogenous factors and then repaired by DNA repair enzymes. Any imbalance in damage and repair and mistakes in repair result in accumulation of DNA damage. Eventually, this will lead to cell death, aging, or cancer. There are several types of DNA lesions. The common ones that can be detected easily are DNA strand breaks and DNA crosslinks. Strand breaks in DNA are produced by endogenous factors, such as free radicals generated by mitochondrial respiration and metabolism, and by exogenous agents, including UV, ionizing and non-ionizing radiation, and chemicals.

There are two types of DNA strand breaks: single- and double-strand breaks. DNA single-strand breaks include frank breaks and alkali labile sites, such as base modification, deamination, depurination, and alkylation. These are the most commonly assessed lesions of DNA. DNA double-strand breaks are very critical for cells and usually they are lethal. DNA strand breaks have been correlated with cell death [1–5], aging [6–8] and cancer [9–13].

Several techniques have been developed to analyze single- and double-strand breaks. Most commonly used is microgel electrophoresis, also called the 'comet assay' or 'single cell gel electrophoresis'. This technique involves mixing cells with agarose, making microgels on a microscope slide, lysing cells in the microgels with salts and detergents, removing proteins from DNA by using proteinase K, unwinding/equilibrating and electrophoresing DNA (under highly alkaline condition for assessment of single-strand breaks or under neutral condition for assessment of DNA double-strand breaks), fixing the DNA, visualizing the DNA with a fluorescent dye, and then analyzing migration patterns of DNA from individual cells with an image analysis system.

The comet assay is a very sensitive method of detecting single- and double-strand breaks if specific criteria are met. Critical criteria include the following. Cells from tissue culture or laboratory animals should be handled with care to minimize DNA damage, for instance, by avoiding light and high temperature. When working with animals exposed to EMF *in vivo*, it is better to anesthetize the animals with CO_2 before harvesting tissues for assay. Antioxidants

* Corresponding author.
E-mail address: jphillip@mail.uccs.edu (J.L. Phillips).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2008.11.005

such as albumin and sucrose, or spin-trap molecules such as α-phenyl-*tert*-butyl nitrone (PBN), should be added during dispersion of tissues into single cells. Cells should be lysed at 0–4 °C to minimize DNA damage by endonucleases. Additionally, antioxidants such as tris and glutathione, and chelators such as EDTA, should be used in the lysing solution. High concentrations of dimethylsulfoxide (DMSO) should be avoided due to its chromatin condensing effect. Treatment with proteinase K (PK; lyophilized DNAse-free proteinase-K from Amresco is ideal) at a concentration of 0.5–1 mg/ml (depending upon cell type and number of cells in the microgel) should be used for 1–2 h at 37 °C to reveal all possible strand breaks which otherwise may go undetected due to DNA–protein crosslinks. Longer times in PK will lead to loss of smaller pieces of DNA by diffusion. Glass slides should be chosen based on which high resolution agarose (3:1 high resolution agarose from Amresco is ideal) will stick well to the slide and on the ability of the specimen to be visualized without excessive fluorescence background. Choice of an electrophoresis unit is important to minimize slide-to-slide variation in DNA migration pattern. A unit with uniform electric field and buffer recirculation should be used. Electrophoresis buffers should have antioxidants and chelators such as DMSO and EDTA. DNA diffusion should be minimized during the neutralization step by rapidly precipitating the DNA. Staining should employ a sensitive fluorescent dye, such as the intercalating fluorescent labeling dye YOYO-1. A cell-selection criteria for analysis should be set before the experiment, such as not analyzing cells with too much damage, although, the number of such cells should be recorded.

There are different versions of the comet assay that have been modified to meet the needs of specific applications and to improve sensitivity. Using the most basic form of the assay, one should be able to detect DNA strand breaks in human lymphocytes that were induced by 5 rad of gamma-ray [14,15].

2. Radiofrequency radiation (RFR) and DNA damage

In a series of publications, Lai and Singh [16–19] reported increases in single- and double-strand DNA breaks, as measured by the comet assay, in brain cells of rats exposed for 2 h to a 2450-MHz RFR at whole body specific absorption rate (SAR) between 0.6 and 1.2 W/kg. The effects were blocked by antioxidants, which suggested involvement of free radicals. At the same time, Sarkar et al. [20] exposed mice to 2450-MHz microwaves at a power density of 1 mW/cm^2 for 2 h/day over a period of 120, 150, and 200 days. Rearrangement of DNA segments were observed in testis and brain of exposed animals. Their data also suggested breakage of DNA strands after RFR exposure. Phillips et al. [21] were the first to study the effects of two forms of cell cellular phone signals, known as TDMA and iDEN, on DNA damage in Molt-4 human lymphoblastoid cells using the comet assay. These cells were exposed to relatively low intensities of the fields (2.4–26 μW/g) for 2–21 h. They reported both increased and decreased DNA damage, depending on the type of signal studied, as well as the intensity and duration of exposure. They speculated that the fields may affect DNA repair in cells. Subsequently, different groups of researchers have also reported DNA damage in various types of cells after exposure to cell phone frequency fields. Diem et al. [22] exposed human fibroblasts and rat granulosa cells to cell phone signal (1800 MHz; SAR 1.2 or 2 W/kg; different modulations; for 4, 16 and 24 h; intermittent 5 min on/10 min off or continuous). RFR exposure induced DNA single- and double-strand breaks as measured by the comet assay. Effects occurred after 16 h of exposure to different cell phone modulations in both cell types. The intermittent exposure schedule caused a significantly stronger effect than continuous exposure. Gandhi and Anita [23] reported increases in DNA strand breaks and micronucleation in lymphocytes obtained from cell phone users. Markova et al. [24] reported that GSM signals affected chromatin conformation and γ-H2AX foci that co-localized in distinct foci with DNA double-strand breaks in human lymphocytes. The effect was found to be dependent on carrier frequency. Nikolova et al. [25] reported a low and transient increase in DNA double-strand breaks in mouse embryonic stem cells after acute exposure to a 1.7-GHz field. Lixia et al. [26] reported an increase in DNA damage in human lens epithelial cells at 0 and 30 min after 2 h of exposure to a 1.8-GHz field at 3 W/kg. Sun et al. [27] reported an increase in DNA single-strand breaks in human lens epithelial cells after 2 h of exposure to a 1.8-GHz field at SARs of 3 and 4 W/kg. DNA damage caused by the field at 4 W/kg was irreversible. Zhang et al. [28] reported that an 1800-MHz field at 3.0 W/kg induced DNA damage in Chinese hamster lung cells after 24 h of exposure. Aitken et al. [29] exposed mice to a 900-MHz RFR at a SAR of 0.09 W/kg for 7 days at 12 h per day. DNA damage in caudal epididymal spermatozoa was assessed by quantitative PCR (QPCR) as well as by alkaline and pulsed-field gel electrophoresis. Gel electrophoresis revealed no significant change in single- or double-strand breaks in spermatozoa. However, QPCR revealed statistically significant damage to both the mitochondrial genome and the nuclear β-globin locus. Changes in sperm cell genome after exposure to 2450-MHz microwaves have also been reported previously by Sarkar et al. [20]. Related to this are several publications that have reported decreased motility and changes in morphology in isolated sperm cells exposed to cell phone radiation [30], sperm cells from animals exposed to cell phone radiation [31], and cell phone users [32–34]. Some of these *in vivo* effects could be caused by hormonal changes [35,36].

There also are studies reporting no significant effect of cell phone RFR exposure on DNA damage. After RFR-induced DNA damage was reported by Lai and Singh [16] using 2450-MHz microwaves and after the report of Phillips et al. [21] on cell phone radiation was published, Motorola funded a series of studies by Roti Roti and colleagues [37] at

Washington University to investigate DNA strand breaks in cells and animals exposed to RFR. None of the studies reported by this group found significant effects of RFR exposure on DNA damage [38–40]. However, a different version of the comet assay was used in these studies. More recently, four additional studies from the Roti-Roti laboratories also reported no significant effects on DNA damage in cells exposed to RFR. Li et al. [41] reported no significant change in DNA strand breaks in murine C3H10T1/2 fibroblasts after 2 h of exposure to 847.74- and 835.02-MHz fields at 3–5 W/kg. Hook et al. [42] showed that a 24-h exposure of Molt-4 cells to CDMA, FDMA, iDEN or TDMA-modulated RFR did not significantly alter the level of DNA damage. Lagroye et al. [43,44] also reported no significant change in DNA strand breaks, protein–DNA crosslinks, and DNA–DNA crosslinks in cells exposed to 2450-MHz RFR.

From other laboratories, Vijayalaxmi et al. [45] reported no increase in DNA stand breaks in human lymphocytes exposed *in vitro* to 2450-MHz RFR at 2.135 W/kg for 2 h. Tice et al. [46] measured DNA single-strand breaks in human leukocytes using the comet assay after exposure to various forms of cell phone signals. Cells were exposed for 3 or 24 h at average SARs of 1.0–10.0 W/kg. Exposure for either 3 or 24 h did not induce a significant increase in DNA damage in leukocytes. McNamee et al. [47–49] found no significant increase in DNA breaks and micronucleus formation in human leukocytes exposed for 2 h to a 1.9-GHz field at SAR up to 10 W/kg. Zeni et al. [50] reported that a 2-h exposure to 900-MHz GSM signal at 0.3 and 1 W/kg did not significantly affect levels of DNA strand breaks in human leukocytes. Sakuma et al. [51] exposed human glioblastoma A172 cells and normal human IMR-90 fibroblasts from fetal lungs to cell phone radiation for 2 and 24 h. No significant changes in DNA strand breaks were observed up to a SAR of 800 mW/kg. Stronati et al. [52] showed that 24 h of exposure to 935-MHz GSM basic signal at 1 or 2 W/Kg did not cause DNA strand breaks in human blood cells. Verschaeve et al. [53] reported that long-term exposure (2 h/day, 5 days/week for 2 years) of rats to 900-MHz GSM signal at 0.3 and 0.9 W/kg did not significantly affect levels of DNA strand breaks in cells.

3. Extremely low frequency electromagnetic fields (ELF EMF) and DNA damage

To complete the picture, a few words on the effects of ELF EMF are required, since cell phones also emit these fields and they are another common form of non-ionizing EMF in our environment. Quite a number of studies have indicated that exposure to ELF EMF could lead to DNA damage [54–69]. In addition, two studies [70,71] have reported effects of ELF fields on DNA repair mechanisms. Free radicals and interaction with transitional metals (e.g., iron) [60,62,63,69] have also been implicated to play a role in the genotoxic effects observed after exposure to these fields.

4. Some considerations on the effects of EMF on DNA

From this brief literature survey, no consistent pattern of RFR exposure inducing changes in or damage to DNA in cells and organisms emerges. However, one can conclude that under certain conditions of exposure, RFR is genotoxic. Data available are mainly applicable only to radiation exposure that would be typical during cell phone use. Other than the study of Phillips et al. [21], there is no indication that RFR at levels that one can experience in the vicinity of base stations and RF-transmission towers could cause DNA damage.

Differences in experimental outcomes are expected since many factors could influence the outcome of experiments in EMF research. Any effect of EMF has to depend on the energy absorbed by a biological organism and on how the energy is delivered in space and time. Frequency, intensity, exposure duration, and the number of exposure episodes can affect the response, and these factors can interact with each other to produce different effects. In addition, in order to understand the biological consequence of EMF exposure, one must know whether the effect is cumulative, whether compensatory responses result, and when homeostasis will break down. The contributions of these factors have been discussed in a talk given by one us (HL) in Vienna, Austria in 1998 [72].

Radiation from cell phone transmission has very complex patterns, and signals vary with the type of transmission. Moreover, the technology is constantly changing. Research results from one types of transmission pattern may not be applicable to other types. Thus, differences in outcomes of the research on genotoxic effects of RFR could be explained by the many different exposure conditions used in the studies. An example is the study of Phillips et al. [21], which demonstrated that different cell phone signals could cause different effects on DNA (i.e., an increase in strand breaks after exposure to one type of signal and a decrease with another). This is further complicated by the fact that some of the studies listed above used poor exposure procedures with very limited documentation of exposure parameters, e.g., using an actual cell phone to expose cells and animals, thus rendering the data from these experiments as questionable.

Another source of influence on experimental outcome is the cell or organism studied. Many different biological systems were used in the genotoxicity studies. Different cell types [73] and organisms [74,75] may not all respond similarly to EMF.

Comment about the comet assay also is required, since it was used in many of the EMF studies to determine DNA damage. Different versions of the assay have been developed. These versions have different detection sensitivities and can be used to measure different aspects of DNA strand breaks. A comparison of data from experiments using different versions of the assay could be misleading. Another concern is that most of the comet assay studies were carried out by experimenters who had no prior experience with this technique and mistakes

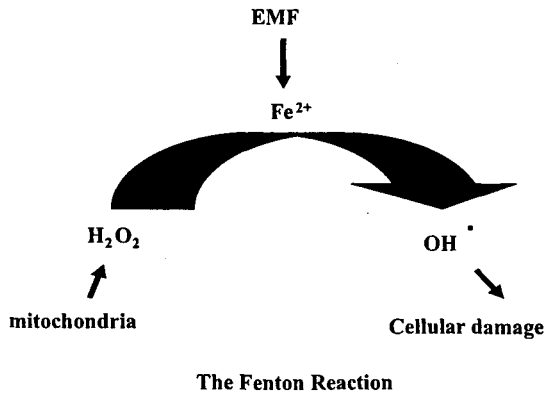


Fig. 1. A representation of the Fenton reaction and its role as a mediator in EMF-induced bioeffects.

were made. For example, in the study by Lagroye et al. [43] to investigate the effect of PK digestion on DNA migration after RFR exposure, PK was added to a lysing solution containing the detergent Triton X-100, which would inactivate the enzyme. Our experience indicates that the comet assay is a very sensitive and requires great care to perform. Thus, different detection sensitivities could result in different laboratories, even if the same procedures are followed. One way to solve this problem of experimental variation is for each research team to report the sensitivity of their comet assay, e.g., the threshold of detecting strand breaks in human lymphocytes exposed to X-rays. This information has generally not been provided for EMF-genotoxicity studies. Interestingly, when such information was provided, a large range of sensitivities have been reported. Malyapa et al. [40] reported a detection level of 0.6 cGy of gamma radiation in human lymphocytes, whereas McNamee et al. [76] reported 10–50 cGy of X-irradiation in lymphocytes, which is much higher than the generally acceptable detection level of the comet assay [15].

A drawback in the interpretation and understanding of experimental data from bioelectromagnetics research is that there is no general acceptable mechanism on how EMF affects biological systems. The mechanism by which EMF produces changes in DNA is unknown. Since the energy level associated with EMF exposure is not sufficient to cause direct breakage of chemical bonds within molecules, the effects are probably indirect and secondary to other induced biochemical changes in cells.

One possibility is that DNA is damaged by free radicals that are formed inside cells. Free radicals affect cells by damaging macromolecules, such as DNA, protein, and membrane lipids. Several reports have indicated that EMF enhances free radical activity in cells [18,19,61,62,77,78], particularly via the Fenton reaction [62]. The Fenton reaction is a process catalyzed by iron in which hydrogen peroxide, a product of oxidative respiration in the mitochondria, is converted into hydroxyl free radicals, which are very potent and cytotoxic molecules (Fig. 1).

It is interesting that ELF EMF has also been shown to cause DNA damage. Furthermore, free radicals have been implicated in this effect of ELF EMF. This further supports the view that EMF affects DNA via an indirect secondary process, since the energy content of ELF EMF is much lower than that of RFR. Effects via the Fenton reaction predict how a cell would respond to EMF. For instance:

(1) Cells that are metabolically active would be more susceptible to EMF, because more hydrogen peroxide is generated by mitochondria to fuel the reaction.
(2) Cells that have high level of intracellular free iron would be more vulnerable to EMF. Cancer cells and cells undergoing abnormal proliferation have higher concentrations of free iron because they uptake more iron and have less efficient iron storage regulation. Thus, these cells could be selectively damaged by EMF. Consequently, this suggests that EMF could potentially be used for the treatment of cancer and hyperplastic diseases. The effect could be further enhanced if one could shift anaerobic glycolysis of cancer cells to oxidative glycolysis. There is quite a large database of information on the effects of EMF (mostly in the ELF range) on cancer cells and tumors. The data tend to indicate that EMF could retard tumor growth and kill cancer cells. One consequence of this consideration is that epidemiological studies of cancer incidence in cell phone users may not show a risk at all or even a protection effect.
(3) Since the brain is exposed to rather high levels of EMF during cell phone use, the consequences of EMF-induced genetic damage in brain cells are of particular importance. Brain cells have high levels of iron. Special molecular pumps are present on nerve cell nuclear membranes to pump iron into the nucleus. Iron atoms have been found to intercalate within DNA molecules. In addition, nerve cells have a low capacity for DNA repair, and DNA breaks could easily accumulate. Another concern is the presence of superparamagnetic iron-particles (magnetites) in body tissues, particularly in the brain. These particles could enhance free radical activity in cells and thus increase the cellular-damaging effects of EMF. These factors make nerve cells more vulnerable to EMF. Thus, the effect of EMF on DNA could conceivably be more significant on nerve cells than on other cell types of the body. Since nerve cells do not divide and are not likely to become cancerous, the more likely consequences of DNA damage in nerve cells include changes in cellular functions and in cell death, which could either lead to or accelerate the development of neurodegenerative diseases. Double-strand breaks, if not properly repaired, are known to lead to cell death. Cumulative DNA damage in nerve cells of the brain has been associated with neurodegenerative diseases, such as Alzheimer's, Huntington's, and Parkinson's diseases. However, another type of brain cell, the glial cell, can become cancerous as a result of DNA damage. The question is whether the damaged cells

would develop into tumors before they are killed by EMF due to over accumulation of genetic damages. The outcome depends on the interplay of these different physical and biological factors—an increase, decrease, or no significant change in cancer risk could result from EMF exposure.

(4) On the other hand, cells with high amounts of antioxidants and antioxidative enzymes would be less susceptible to EMF. Furthermore, the effect of free radicals could depend on the nutritional status of an individual, e.g., availability of dietary antioxidants, consumption of alcohol, and amount of food consumption. Various life conditions, such as psychological stress and strenuous physical exercise, have been shown to increase oxidative stress and enhance the effect of free radicals in the body. Thus, one can also speculate that some individuals may be more susceptible to the effects of EMF exposure.

Additionally, the work of Blank and Soo [79] and Blank and Goodman [80] support the possibility that EMF exposure at low levels has a direct effect on electron transfer processes. Although the authors do not discuss their work in the context of EMF-induced DNA damage, the possibility exists that EMF exposure could produce oxidative damage to DNA.

5. Lessons learned

Whether or not EMF causes biological effects, let alone effects that are detrimental to human health and development, is a contentious issue. The literature in this area abounds with apparently contradictory studies, and as presented in this review, the literature specific to the effects of RFR exposure on DNA damage and repair in various biological systems is no exception. As a consequence of this controversy, there are several key issues that must be addressed—contrary data, weight of evidence, and data interpretation consistent with known science.

Consider that EMF does not share the familiar and comforting physical properties of chemical agents. EMF cannot be seen, tasted, smelled, or felt (except at high intensities). It is relevant, therefore, to ask, in what ways do scientists respond to data, especially if that data are contrary to their scientific beliefs or inconsistent with long-held hypotheses? Often such data are ignored, simply because it contradict what is accepted as conventional wisdom. Careful evaluation and interpretation of data may be difficult, because technologies used to expose biological systems to EMF and methodologies used to assess dosimetry generally are outside the experience of most biomedical scientists. Additionally, it is often difficult to assess differences in methodologies between studies, one or more of which were intended to replicate an original investigation. For instance, Malyapa et al. [40] reported what they claimed to be a replication of the work of Lai and Singh [16]. There were, however, significant differences in the comet analyses used by each group. Lai and Singh precipitated DNA in agarose so that low levels of DNA damage could be detected. Malyapa et al. did not. Lai and Singh treated their samples with PK to digest proteins bound to DNA, thus allowing DNA to move toward the positive pole during electrophoresis (unlike DNA, most proteins are negatively charged, and if they are not removed they will drag the DNA toward the negative pole). The Malyapa et al. study did not use PK. There were other methodological differences as well. Such is also the case in the study of Hook et al. [42], which attempted to replicate the work of Phillips et al. [21]. The latter group used a PK treatment in their comet assay, while the former group did not.

While credibility is enhanced when one can relate data to personal knowledge and scientific beliefs, it has not yet been determined how RFR couples with biological systems or by what mechanisms effects are produced. Even carefully designed and well executed RFR exposure studies may be summarily dismissed as methodologically unsound, or the data may be interpreted as invalid because of inconsistencies with what one believes to be correct. The quintessential example is the belief that exposure to RFR can produce no effects that are not related to the ability of RFR to produce heat, that is, to raise the temperature of biological systems [81,82]. Nonetheless, there are many examples of biological effects resulting from low-level (athermal) RFR exposure [83,84]. Consider here the work of Mashevich et al. [85]. This group exposed human peripheral blood lymphocytes to an 830-MHz signal for 72 h and at different average SARs (SAR, 1.6–8.8 W/kg). Temperatures ranged from 34.5 to 38.5 °C. This group observed an increase in chromosome 17 aneuploidy that varied linearly with SAR. Temperature elevation alone in the range of 34.5–38.5 °C did not produce this genotoxic effect, although significant aneuploidy was observed at higher temperatures of 40–41 °C. The authors conclude that the genotoxic effect of the radiofrequency signal used is elicited through a non-thermal pathway.

Also consider one aspect of the work of Phillips et al. [21]. In that study, DNA damage was found to vary in direction; that is, under some conditions of signal characteristics, signal intensity, and time of exposure, DNA damage increased as compared with concurrent unexposed controls, while under other conditions DNA damage decreased as compared with controls. The dual nature of Phillips et al.'s [21] results will be discussed later. For now consider the relationship of these results to other investigations. Adey et al. [86] performed an *in vivo* study to determine if rats treated *in utero* with the carcinogen ethylnitrosourea (ENU) and exposed to an 836.55-MHz field with North American Digital Cellular modulation (referred to as a TDMA field) would develop increased numbers of central system tumors. This group reported that rather than seeing an increase in tumor incidence in RFR-exposed rats, there was instead a decrease in tumor incidence. Moreover, rats that received no ENU but which were exposed to the TDMA signal also showed a decrease in the number of spontaneous tumors as compared

with animals exposed to neither ENU nor the TDMA signal. This group postulated that their results may be mechanistically similar to the work of another group. Stammberger et al. [87] had previously reported that rats treated *in utero* with ENU and then exposed to low doses of X-irradiation exhibited significantly reduced incidences of brain tumors in adult life. Stammberger and colleagues [87] hypothesized that low-level X-irradiation produced DNA damage that then induced the repair enzyme 0^6-alkylguanine-DNA alkyltransferase (AT). Numerous groups have since reported that X-irradiation does indeed induce AT activity (e.g., [88,89]). In this context, it is significant that Phillips et al. [21] found that cells exposed *in vitro* to a TDMA signal identical to that used in the study of Adey et al. [86] produced a decrease in DNA damage under specific conditions of intensity and time of exposure (lower intensity, longer time; higher intensity, shorter time). These results raise the intriguing possibility that the decrease in tumor incidence in the study of Adey et al. [86] and the decrease in DNA damage in the study of Phillips et al. [21] both may have been the result of induction of AT activity resulting from DNA damage produced by exposure to the TDMA signal. This remains to be investigated.

Because the issue of RFR-induced bioeffects is contentious, and because the issue is tried in courtrooms and various public forums, a term heard frequently is weight of evidence. This term generally is used to describe a method by which all scientific evidence related to a causal hypothesis is considered and evaluated. This process is used extensively in matters of regulation, policy, and the law, and it provides a means of weighing results across different modalities of evidence. When considering the effects of RFR exposure on DNA damage and repair, modalities of evidence include studies of cells and tissues from laboratory animals exposed *in vivo* to RFR, studies of cells from humans exposed to RFR *in vivo*, and studies of cells exposed *in vitro* to RFR. While weight of evidence is gaining favor with regulators [90], its application by scientists to decide matters of science is often of questionable value. One of the reasons for this is that there generally is no discussion or characterization of what weight of evidence actually means in the context in which it is used. Additionally, the distinction between weight of evidence and strength of evidence often is lacking or not defined, and differences in methodologies between investigators are not considered. Consequently, weight of evidence generally amounts to what Krimsky [90] refers to as a "seat-of-the-pants qualitative assessment." Krimsky points out that according to this view, weight of evidence is "a vague term that scientists use when they apply implicit, qualitative, and/or subjective criteria to evaluate a body of evidence." Such is the case in the reviews by Juutilainen and Lang [91] and Verschaeve and Maes [92]. There is little emphasis on a critical analysis of similarities and differences in biological systems used, exposure regimens, data produced, and investigator's interpretations and conclusions. Rather, there is greater emphasis on the number of publications either finding or not finding an effect of RFR exposure on some endpoint. To some investigators, weight of evidence does indeed refer to the balance (or imbalance) between the number of studies producing apparently opposing results, without regard to critical experimental variables. While understanding the role these variables play in determining experimental outcome could provide remarkable insights into defining mechanisms by which RFR produced biological effects, few seem interested in or willing to delve deeply into the science.

A final lesson can be derived from a statement made by Gos et al. [93] referring to the work of Phillips et al. [21]. Gos and colleagues state, "The results in the latter study (Phillips et al., 1998) are puzzling and difficult to interpret, as no consistent increase or decrease in signal in the comet assay at various SARs or times of exposure was identified." This statement is pointed out because studies of the biological effects of exposure to electromagnetic fields at any frequency are often viewed as outside of or distinct from what many refer to as *mainstream science*. However, what has been perceived as an inconsistent effect is indeed consistent with the observations of bimodal effects reported in hundreds of peer-reviewed publications. These bimodal effects may be dependent on concentration of an agent, time of incubation with an agent, or some other parameter relating to the state of the system under investigation. For instance, treatment of B cells for a short time (30 min) with the protein kinase C activator phorbol 12,13-dibutyrate increased proliferative responses to anti-immunoglobulin antibody, whereas treatment for a longer period of time ($\geq$3 h) suppressed proliferation [94]. In a study of κ-opioid agonists on locomotor activity in mice, Kuzmin et al. [95] reported that higher, analgesic doses of κ-agonists reduced rearing, motility, and locomotion in non-habituated mice. In contrast, lower, subanalgesic doses increased motor activity in a time-dependent manner. Dierov et al. [96] observed a bimodal effect of all-trans-retinoic acid (RA) on cell cycle progression in lymphoid cells that was temporally related to the length of exposure to RA. A final example is found in the work of Rosenstein et al. [97]. This group found that the activity of melatonin on depolarization-induced calcium influx by hypothalamic synaptosomes from rats sacrificed late evening (2000 h) depended on melatonin preincubation time. A short preincubation time (10 min) stimulated uptake, while a longer preincubation (30 min) inhibited calcium uptake. These effects were also dependent on the time of day when the rats were sacrificed. Effects were maximal at 2000 h, minimal at 2400 h, and intermediate at 400 h. At 1000 h, only inhibitory effects of melatonin on calcium uptake were observed. These examples point out that what appears to be inconsistency may instead be real events related to and determined by the agents involved and the state of the biological system under investigation. The results of Phillips et al. [21] may be the result of signal modulation, signal intensity, time of exposure, or state of the cells. The results may indicate a bimodal effect, or they may, as the investigators suggest, represent time- and signal-dependant changes in the balance between damage and repair because of direct or indirect effects of RFR exposure on repair mechanisms.

6. Summary

Exposure of laboratory animals *in vivo* and of cultured cells *in vitro* to various radiofrequency signals has produced changes in DNA damage in some investigations and not in others. That many of the studies on both sides of this issue have been done well is encouraging from a scientific perspective. RFR exposure does indeed appear to affect DNA damage and repair, and the total body of available data contains clues as to conditions producing effects and methodologies to detect them. This view is in contrast to that of those who believe that studies unable to replicate the work of others are more credible than the original studies, that studies showing no effects cancel studies showing an effect, or that studies showing effects are not credible simply because we do not understand how those effects might occur. Some may be tempted to apply incorrectly the teachings of Sir Karl Popper, one of the great science philosophers of the 20th century. Popper proposed that many examples may lend support to an hypothesis, while only one negative instance is required to refute it [98]. While this holds most strongly for logical subjects, such as mathematics, it does not hold well for more complex biological phenomena that are influenced by stochastic factors. Each study to investigate RFR-induced DNA damage must be evaluated on its own merits, and then studies that both show effects and do not show effects must be carefully evaluated to define the relationship of experimental variables to experimental outcomes and to assess the value of experimental methodologies to detect and measure these outcomes (see Section 2).

The lack of a causal or proven mechanism(s) to explain RFR-induced effects on DNA damage and repair does not decrease the credibility of studies in the scientific literature that report effects of RFR exposure, because there are several plausible mechanisms of action that can account for the observed effects. The relationship between cigarette smoking and lung cancer was accepted long before a mechanism was established. This, however, occurred on the strength of epidemiologic data [99]. Fortunately, relevant epidemiologic data relating long-term cell phone use (>10 years) to central nervous system tumors are beginning to appear [84,100–102], and these data point to an increased risk of acoustic neuroma, glioma and parotid gland tumors.

One plausible mechanism for RFR-induced DNA damage is free radical damage. After finding that two free radical scavengers (melatonin and N-tert-butyl-α-phenylnitrone) prevent RFR-induced DNA damage in rat brain cells, Lai and Singh [62] hypothesized that this damage resulted from free radical generation. Subsequently, other reports appeared that also suggested free radical formation as a result of RFR exposure [103–105]. Additionally, some investigators have reported that non-thermal exposure to RFR alters protein structure and function [106–109]. Scientists are familiar with molecules interacting with proteins through lock-and-key or induced-fit mechanisms. It is accepted that such interactions provide energy to change protein conformation and protein function. Indeed, discussions of these principles are presented in introductory biology and biochemistry courses. Perhaps then it is possible that RFR exposure, in a manner similar to that of chemical agents, provides sufficient energy to alter the structure of proteins involved in DNA repair mechanisms to the extent that their function also is changed. This has not yet been investigated.

When scientists maintain their beliefs in the face of contrary data, two diametrically opposed situations may result. On the one hand, data are seen as either right or wrong and there is no discussion to resolve disparities. On the other hand, and as Francis Crick [110] has pointed out, scientists who hold theoretically opposed positions may engage in fruitful debate to enhance understanding of underlying principles and advance science in general. While the latter certainly is preferable, there are external factors involving economics and politics that keep this from happening. It is time to acknowledge this and embark on the path of fruitful discussion. Great scientific discoveries await.

Acknowledgment

We thank Khushbu Komal and Ji-Sun Park for assistance in the preparation of the manuscript.

References

[1] J.F. Ward, The yield of DNA double strand breaks produced intracellularly by ionizing radiation: a review, Int. J. Radiat. Biol. 57 (1990) 1141–1150.
[2] P.R. Walker, C. Smith, T. Youdale, J. Leblanc, J.F. Whitfield, M. Sikorska, Topoisomerase II-reactive chemotherapeutic drugs induce apoptosis in thymocytes, Cancer Res. 51 (1991) 1078–1085.
[3] Y. Onishi, Y. Azuma, Y. Sato, Y. Mizuno, T. Tadakuma, H. Kizaki, Topoisomerase inhibitors induce apoptosis in thymocytes, Biochem. Biophys. Acta 1175 (1993) 147–154.
[4] P. Prigent, C. Blanpied, J. Aten, F. Hirsch, A safe and rapid method for analyzing apoptosis-induced fragmentation of DNA extracted from tissues or cultured cells, J. Immunol. Methods 160 (1993) 139–140.
[5] K. Schindowski, S. Leutner, W.E. Muller, A. Eckert, Age related changes of apoptotic cell death in human lymphocytes, Neurobiol. Aging 21 (2000) 661–670.
[6] R.W. Hart, R.B. Setlow, Correlation between deoxyribonucleic acid excision repair and life span in a number of mammalian species, Proc. Natl. Acad. Sci. U.S.A. 71 (1974) 2169–2173.
[7] M.R. Lieber, Pathological and physiological double-strand breaks: roles in cancer, aging, and theimmune system, Am. J. Pathol. 153 (1998) 1323–1332.
[8] H. Li, J.R. Mitchell, P. Hasty, DNA double-strand breaks: a potential causative factor for mammalian aging, Mech. Aging Dev. 129 (2008) 416–424.
[9] R.R. R.R.Tice, Aging and DNA repair capability, in: E.L. Schneider (Ed.), The Genetics of Aging, Plenum Press, New York, 1978, pp. 53–89.
[10] P.A. Cerutti, Peroxidant states and tumor promotion, Science 227 (1985) 375–381.
[11] B.N. Ames, Endogenous DNA damage as related to cancer and aging, Mutat. Res. 214 (1989) 41–46.

[12] B.N. Ames, Endogenous oxidative DNA damage, aging, and cancer, Free Radical Res. Commun. 7 (1989) 121–128.
[13] T. Helleday, J. Loc, D.C. van Gentd, B.P. Engelward, DNA double-strand break repair: from mechanistic understanding to cancer treatment, DNA Repair 6 (2007) 923–935.
[14] R.B. Jarvis, J.F. Knowles, DNA damage in Zebrafish larvae induced by exposure to low-dose rate gamma-radiation: detection by the alkaline comet assay, Mutat. Res. 541 (2003) 63–69.
[15] R.R. Tice, G.H. Strauss, The single cell gel electrophoresis/comet assay: a potential tool for detecting radiation-induced DNA damage in humans, Stem Cells. Suppl. 1 (1995) 207–214.
[16] H. Lai, N.P. Singh, Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells, Bioelectromagnetics 16 (1995) 207–210.
[17] H. Lai, N.P. Singh, Single and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation, Int. J. Radiat. Biol. 69 (1996) 513–521.
[18] H. Lai, N.P. Singh, Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells, Bioelectromagnetics 18 (1997) 446–454.
[19] H. Lai, N.P. Singh, Effects of microwaves and a temporally incoherent magnetic field on single and double DNA strand breaks in rat brain cells, Electromag. Biol. Med. 24 (2005) 23–29.
[20] S. Sarkar, S. Ali, J. Behari, Effect of low power microwave on the mouse genome: a direct DNA analysis, Mutat. Res. 320 (1994) 141–147.
[21] J.L. Phillips, O. Ivaschuk, T. Ishida-Jones, R.A. Jones, M. Campbell-Beachler, W. Haggren, DNA damage in Molt-4 T- lymphoblastoid cells exposed to cellular telephone radiofrequency fields *in vitro*, Bioelectrochem. Bioenerg. 45 (1998) 103–110.
[22] E. Diem, C. Schwarz, F. Adlkofer, O. Jahn, H. Rudiger, Non-thermal DNA breakage by mobile-phone radiation (1800-MHz) in human fibroblasts and in transformed GFSH-R17 rat granulosa cells in vitro, Mutat. Res. 583 (2005) 178–183.
[23] G. Gandhi, Anita, Genetic damage in mobile phone users: some preliminary findings, Indian J. Hum. Genet. 11 (2005) 99–104.
[24] E. Markova, L. Hillert, L. Malmgren, B.R. Persson, I.Y. Belyaev, Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons, Environ. Health Perspect. 113 (2005) 1172–1177.
[25] T. Nikolova, J. Czyz, A. Rolletschek, P. Blyszczuk, J. Fuchs, G. Jovtchev, J. Schuderer, N. Kuster, A.M. Wobus, Electromagnetic fields affect transcript levels of apoptosis-related genes in embryonic stem cell-derived neural progenitor cells, FASEB J. 19 (2005) 1686–1688.
[26] S. Lixia, K. Yao, W. Kaijun, L. Deqiang, H. Huajun, G. Xiangwei, W. Baohong, Z. Wei, L. Jianling, W. Wei, Effects of 1.8-GHz radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells, Mutat. Res. 602 (2006) 135–142.
[27] L.X. Sun, K. Yao, J.L. He, D.Q. Lu, K.J. Wang, H.W. Li, Effect of acute exposure to microwave from mobile phone on DNA damage and repair of cultured human lens epithelial cells in vitro, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 24 (2006) 465–467.
[28] D.Y. Zhang, Z.P. Xu, H. Chiang, D.Q. Lu, Q.L. Zeng, Effects of GSM 1800 MHz radiofrequency electromagnetic fields on DNA damage in Chinese hamster lung cells, Zhonghua Yu Fang Yi Xue Za Zhi 40 (2006) 149–152.
[29] R.J. Aitken, L.E. Bennetts, D. Sawyer, A.M. Wiklendt, B.V. King, Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline, Int. J. Androl. 28 (2005) 171–179.
[30] O. Erogul, E. Oztas, I. Yildirim, T. Kir, E. Aydur, G. Komesli, H.C. Irkilata, M.K. Irmak, A.F. Peker, Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study, Arch. Med. Res. 37 (2006) 840–843.
[31] J.G. Yan, M. Agresti, T. Bruce, Y.H. Yan, A. Granlund, H.S. Matloub, Effects of cellular phone emissions on sperm motility in rats, Fertil. Steril. 88 (2007) 957–964.
[32] A. Agarwal, F. Deepinder, R.K. Sharma, G. Ranga, J. Li, Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study, Fertil. Steril. 89 (2008) 124–128.
[33] I. Fejes, Z. Za Vaczki, J. Szollosi, R.S. Kolosza, J. Daru, C.L. Kova, L.A. Pa, Is there a relationship between cell phone use and semen quality? Arch. Androl. 51 (2005) 385–393.
[34] A. Wdowiak, L. Wdowiak, H. Wiktor, Evaluation of the effect of using mobile phones on male fertility, Ann. Agric. Environ. Med. 14 (2007) 169–172.
[35] Z. Forgacs, Z. Somosy, G. Kubinyi, J. Bakos, A. Hudak, A. Surjan, G. Thuroczy, Effect of whole-body 1800 MHz GSM-like microwave exposure on testicular steroidogenesis and histology in mice, Reprod. Toxicol. 22 (2006) 111–117.
[36] M. Ozguner, A. Koyu, G. Cesur, M. Ural, F. Ozguner, A. Gokcimen, N. Delibas, Biological and morphological effects on the reproductive organ of rats after exposure to electromagnetic field, Saudi Med. J. 26 (2005) 405–410.
[37] J.L. Roti Roti, R.S. Malyapa, K.S. Bisht, E.W. Ahern, E.G. Moros, W.F. Pickard, W.L. Straube, Neoplastic transformation in C3H 10T(1/2) cells after exposure to 835.62 MHz FDMA and 847.74 MHz CDMA radiations, Radiat. Res. 155 (2001) 239–247.
[38] R.S. Malyapa, E.W. Ahern, W.L. Straube, E.G. Moros, W.F. Pickard, J.L. Roti Roti, Measurement of DNA damage after exposure to 2450 MHz electromagnetic radiation, Radiat. Res. 1481 (1997) 608–617.
[39] R.S. Malyapa, E.W. Ahern, W.L. Straube, E.G. Moros, W.F. Pickard, J.L. Roti Roti, Measurement of DNA damage after exposure to electromagnetic radiation in the cellular phone communication frequency band (835.62 and 847.74 MHz), Radiat. Res. 148 (1997) 618–627.
[40] R.S. Malyapa, C. Bi, E.W. Ahern, J.L. Roti Roti, Detection of DNA damage by the alkaline comet assay after exposure to low-dose gamma radiation, Radiat. Res. 149 (1998) 396–400.
[41] L. Li, K.S. Bisht, I. LaGroye, P. Zhang, W.L. Straube, E.G. Moros, J.L. Roti Roti, Measurement of DNA damage in mammalian cells exposed in vitro to radiofrequency fields at sars of 3–5 W/kg, Radiat. Res. 156 (2001) 328–332.
[42] G.J. Hook, P. Zhang, I. Lagroye, L. Li, R. Higashikubo, E.G. Moros, W.L. Straube, W.F. Pickard, J.D. Baty, J.L. Roti Roti, Measurement of DNA damage and apoptosis in molt-4 cells after in vitro exposure to radiofrequency radiation, Radiat. Res. 161 (2004) 193–200.
[43] I. Lagroye, R. R.Anane, B.A. Wettring, E.G. E.G.Moros, W.L. Straube, M. Laregina, M. Niehoff, W.F. Pickard, J. Baty, J.L. Roti, Measurement of DNA damage after acute exposure to pulsed-wave 2450 MHz microwaves in rat brain cells by two alkaline comet assay methods, Int. J. Radiat. Biol. 80 (2004) 11–20.
[44] I. Lagroye, G.J. Hook, B.A. Wettring, J.D. Baty, E.G. Moros, W.L. Straube, J.L. Roti Roti, Measurements of alkali-labile DNA damage and protein-DNA crosslinks after 2450 MHz microwave and low-dose gamma irradiation in vitro, Radiat. Res. 161 (2004) 201–214.
[45] Vijayalaxmi, B.Z. Leal, M. Szilagyi, T.J. Prihoda, M.L. Meltz, Primary DNA damage in human blood lymphocytes exposed in vitro to 2450 MHz radiofrequency radiation, Radiat. Res. 153 (2000) 479–486.
[46] R.R. Tice, G.G. Hook, M. Donner, D.I. McRee, A.W. Guy, Genotoxicity of radiofrequency signals. I. Investigation of DNA damage and micronuclei induction in cultured human blood cells, Bioelectromagnetics 23 (2002) 113–126.
[47] J.P. McNamee, P.V. Bellier, G.B. Gajda, S.M. Miller, E.P. Lemay, B.F. Lavallee, L. Marro, A. Thansandote, DNA damage and micronucleus induction in human leukocytes after acute in vitro exposure to a 1.9 GHz continuous-wave radiofrequency field, Radiat. Res. 158 (2002) 523–533.
[48] J.P. McNamee, P.V. Bellier, G.B. Gajda, B.F. Lavallee, E.P. Lemay, L. Marro, A. Thansandote, DNA damage in human leukocytes after acute in vitro exposure to a 1.9 GHz pulse-modulated radiofrequency field, Radiat. Res. 158 (2002) 534–537.

[49] J.P. McNamee, P.V. Bellier, G.B. Gajda, B.F. Lavallee, L. Marro, E. Lemay, A. Thansandote, No evidence for genotoxic effects from 24 h exposure of human leukocytes to 1.9 GHz radiofrequency fields, Radiat. Res. 159 (2003) 693–697.

[50] O. Zeni, M. Romano, A. Perrotta, M.B. Lioi, R. Barbieri, G. d'Ambrosio, R. Massa, M.R. Scarfi, Evaluation of genotoxic effects in human peripheral blood leukocytes following an acute in vitro exposure to 900 MHz radiofrequency fields, Bioelectromagnetics 26 (2005) 258–265.

[51] N. Sakuma, Y. Komatsubara, H. Takeda, H. Hirose, M. Sekijima, T. Nojima, J. Miyakoshi, DNA strand breaks are not induced in human cells exposed to 2.1425 GHz band CW and W-CDMA modulated radiofrequency fields allocated to mobile radio base stations, Bioelectromagnetics 27 (2006) 51–57.

[52] L. Stronati, A. Testa, J. Moquet, A. Edwards, E. Cordelli, P. Villan, C. Marino, A.M. Fresegna, M. Appolloni, D. Lloyd, 935 MHz cellular phone radiation. An in vitro study of genotoxicity in human lymphocytes, Int. J. Radiat. Biol. 82 (2006) 339–346.

[53] L. Verschaeve, P. Heikkinen, G. Verheyen, U. Van Gorp, F. Boonen, F. Vander Plaetse, A. Maes, T. Kumlin, J. Maki-Paakkanen, L. Puranen, J. Juutilainen, Investigation of co-genotoxic effects of radiofrequency electromagnetic fields in vivo, Radiat. Res. 165 (2006) 598–607.

[54] Y.R. Ahuja, B. Vijayashree, R. Saran, E.L. Jayashri, J.K. Manoranjani, S.C. Bhargava, In vitro effects of low-level, low-frequency electromagnetic fields on DNA damage in human leucocytes by comet assay, Indian J. Biochem. Biophys. 36 (1999) 318–322.

[55] J. Delimaris, S. Tsilimigaki, N. Messini-Nicolaki, E. Ziros, S.M. Piperakis, Effects of pulsed electric fields on DNA of human lymphocytes, Cell Biol. Toxicol. 22 (2006) 409–415.

[56] R. Hong, Y. Zhang, Y. Liu, E.Q. Weng, Effects of extremely low frequency electromagnetic fields on DNA of testicular cells and sperm chromatin structure in mice, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 23 (2005) 414–417.

[57] S. Ivancsits, E. Diem, A. Pilger, H.W. Rudiger, O. Jahn, Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts, Mutat. Res. 519 (2002) 1–13.

[58] S. Ivancsits, E. Diem, O. Jahn, H.W. Rudiger, Age-related effects on induction of DNA strand breaks by intermittent exposure to electromagnetic fields, Mech. Aging Dev. 124 (2003) 847–850.

[59] S. Ivancsits, A. Pilger, E. Diem, O. Jahn, H.W. Rudiger, Cell type-specific genotoxic effects of intermittent extremely low-frequency electromagnetic fields, Mutat. Res. 583 (2005) 184–188.

[60] J. Jajte, M. Zmyslony, J. Palus, E. Dziubaltowska, E. Rajkowska, Protective effect of melatonin against in vitro iron ions and 7 mT 50 Hz magnetic field-induced DNA damage in rat lymphocytes, Mutat. Res. 483 (2001) 57–64.

[61] H. Lai, N.P. Singh, Melatonin, N-tert-butyl-alpha-phenylnitrone block 60-Hz magnetic field-induced DNA single and double strand breaks in rat brain cells, J. Pineal. Res. 22 (1997) 152–162.

[62] H. Lai, N.P. Singh, Magnetic-field-induced DNA strand breaks in brain cells of the rat, Environ. Health Perspect. 112 (2004) 687–694.

[63] R. Lourencini da Silva, F. Albano, L.R. Lopes dos Santos, A.D. Tavares Jr., I. Felzenszwalb, The effect of electromagnetic field exposure on the formation of DNA lesions, Redox. Rep. 5 (2000) 299–301.

[64] C. Schmitz, E. Keller, T. Freuding, J. Silny, H. Korr, 50-Hz magnetic field exposure influences DNA repair and mitochondrial DNA synthesis of distinct cell types in brain and kidney of adult mice, Acta Neuropathol. (Berl) 107 (2004) 257–264.

[65] B.M. Svedenstal, K.J. Johanson, K.H. Mild, DNA damage induced in brain cells of CBA mice exposed to magnetic fields, In Vivo 13 (1999) 551–552.

[66] R. Winker, S. Ivancsits, A. Pilger, F. Adlkofer, H.W. Rudiger, Chromosomal damage in human diploid fibroblasts by intermittent exposure to extremely low-frequency electromagnetic fields, Mutat. Res. 585 (2005) 43–49.

[67] F.I. Wolf, A. Torsello, B. Tedesco, S. Fasanella, A. Boninsegna, M. D'Ascenzo, C. Grassi, G.B. Azzena, A. Cittadini, 50-Hz extremely low frequency electromagnetic fields enhance cell proliferation and DNA damage: possible involvement of a redox mechanism, Biochim. Biophys. Acta 1743 (2005) 120–129.

[68] B. Yokus, D.U. Cakir, M.Z. Akdag, C. Sert, N. Mete, Oxidative DNA damage in rats exposed to extremely low frequency electro magnetic fields, Free Radic. Res. 39 (2005) 317–323.

[69] M. Zmyslony, J. Palus, J. Jajte, E. Dziubaltowska, E. Rajkowska, DNA damage in rat lymphocytes treated in vitro with iron cations and exposed to 7 mT magnetic fields (static or 50 Hz), Mutat. Res. 453 (2000) 89–96.

[70] K. Chow, W.L. Tung, Magnetic field exposure enhances DNA repair through the induction of DnaK/J synthesis, FEBS Lett. 478 (2000) 133–136.

[71] J.G. Robison, A.R. Pendleton, K.O. Monson, B.K. Murray, K.L. O'Neill, Decreased DNA repair rates and protection from heat induced apoptosis mediated by electromagnetic field exposure, Bioelectromagnetics 23 (2002) 106–112.

[72] H. Lai, Neurological effects of radiofrequency electromagnetic radiation, in: Mobile Phones and Health, Symposium, October 25–28, University of Vienna, Austria, 1998, see: http://www.waveguide.org/library/lai.html.

[73] A. Höytö, J. Juutilainen, J. Naarala, Ornithine decarboxylase activity is affected in primary astrocytes but not in secondary cell lines exposed to 872 MHz RF radiation, Int. J. Radiat. Biol. 83 (2007) 367–374.

[74] L.E. Anderson, J.E. Morris, L.B. Sasser, W. Löscher, Effects of 50- or 60-hertz, 100 microT magnetic field exposure in the DMBA mammary cancer model in Sprague-Dawley rats: possible explanations for different results from two laboratories, Environ. Health Perspect. 108 (2000) 797–802.

[75] A.L. Di Carlo, T.A. Litovitz, Is genetics the unrecognized confounding factor in bioelectromagnetics? Flock-dependence of field-induced anoxia protection in chick embryos, Bioelectrochem. Bioenerg. 48 (1999) 209–215.

[76] J.P. McNamee, J.R. McLean, C.L. Ferrarotto, P.V. Bellier, Comet assay: rapid processing of multiple samples, Mutat. Res. 466 (2000) 63–69.

[77] B. Oral, M. Guney, F. Ozguner, N. Karahan, T. Mungan, S. Comlekci, G. Cesur, Endometrial apoptosis induced by a 900-MHz mobile phone: preventive effects of vitamins E and C, Adv. Ther. 23 (2006) 957–973.

[78] M. Simkó, Cell type specific redox status is responsible for diverse electromagnetic field effects, Curr. Med. Chem. 14 (2007) 1141–1152.

[79] M. Blank, L. Soo, Electromagnetic acceleration of the Belousov-Zhabotinski reaction, Bioelectrochemistry 61 (2003) 93–97.

[80] M. Blank, R. Goodman, A mechanism for stimulation of biosynthesis by electromagnetic fields: charge transfer in DNA and base pair separation, J. Cell. Physiol. 214 (2008) 20–26.

[81] K.R. Foster, R. Glaser, Thermal mechanisms of interaction of radiofrequency energy with biological systems with relevance to exposure guidelines, Health Phys. 92 (2007) 609–620.

[82] A. Peter, T. Valberg, E. van Deventer, M.H. Repacholi, Workgroup Report: Base Stations and Wireless Networks—Radiofrequency (RF) Exposures and Health Consequences, Environ. Health Perspect. 115 (2007) 416–424.

[83] D. Krewski, B.W. Glickman, R.W. Habash, B. Habbick, W.G. Lotz, R. Mandeville, F.S. Prato, T. Salem, D.F. Weaver, Recent advances in research on radiofrequency fields and health: 2001–2003, J. Toxicol. Environ. Health, Part B 10 (2007) 287–318.

[84] L. Hardell, M. Carlberg, F. Soderqvist, K.H. Mild, L.L. Morgan, Long-term use of cellular phones and brain tumors: increased risk associated with use for ≥10 years, Occup. Environ. Med. 64 (2007) 626–632.

[85] M. Mashevich, D. Folkman, A. Kesar, A. Barbul, R. Korenstein, E. Jerby, L. Avivi, Exposure of human peripheral blood lymphocytes to electromagnetic fields associated with cellular phones leads to chromosomal instability, Bioelectromagnetics 24 (2003) 82–90.

[86] W. Adey, C. Byus, C. Cain, R. Higgins, R. Jones, Spontaneous and nitrosourea-induced primary tumors of the central nervous system in Fischer 344 rats chronically exposed to 836 MHz modulated microwaves, Radiat. Res. 152 (1999) 293–302.

[87] J. Stammberger, W. Schmahl, L. Nice, The effects of X-irradiation, N-ethyl-N-nitrosourea or combined treatment on 0^6-alkylguanine-DNA alkyltransferase activity in fetal rat brain and liver and the induction of CNS tumors, Carcinogenesis 11 (1990) 219–222.

[88] J.A. Rafferty, A.R. Clarke, D. Sellappan, M.S. Koref, I.M. Frayling, G.P. Margison, Induction of murine O6-alkylguanine-DNA-alkyltransferase in response to ionising radiation is p53 gene dose dependent, Oncogene 12 (1996) 693–697.

[89] T. Grombacher, U. Eichhorn, B. Kaina, p53 is involved in regulation of the DNA repair gene O6-methylguanine-DNA methyltransferase (MGMT) by DNA damaging agents, Oncogene 17 (1998) 845–851.

[90] S. Krimsky, The weight of scientific evidence in policy and law, Am. J. Public Health 95 (2005) S129–S136.

[91] J. Juutilainen, S. Lang, Genotoxic, carcinogenic, and teratogenic effects of electromagnetic fields, Introduction and overview, Mutat. Res 387 (1997) 165–171.

[92] L. Verschaeve, A. Maes, Genetic, carcinogenic and teratogenic effects of radiofrequency fields, Mutat. Res. 410 (1998) 141–165.

[93] P. Gos, B. Eicher, J. Kohli, W.D. Heyer, No mutagenic or recombinogenic effects of mobile phone fields at 900 MHz detected in the yeast *saccharomyces cerevisiae*, Bioelectromagnetics 21 (2000) 515–523.

[94] J.J. Mond, N. Feuerstein, C.H. June, A.K. Balapure, R.I. Glazer, K. Witherspoon, M. Brunswick, Bimodal effect of phorbol ester on B cell activation, J. Biol. Chem. 266 (1991) 4458–4463.

[95] A. Kuzmin, J. Sandin, L. Terenius, S.O. Ogren, Dose- and time-dependent bimodal effects of k-opioid agonists on locomotor activity in mice, J. Pharmacol. Exp. Ther. 295 (2000) 1031–1042.

[96] J. Dierov, B.E. Sawaya, M. Prosniak, R.B. Gartenhaus, Retinoic acid modulates a bimodal effect on cell cycle progression in human adult T-cell leukemia cell, Clin. Cancer Res. 5 (1999) 2540–2547.

[97] R.E. Rosenstein, D.A. Golombek, B.I. Kanterewicz, D.P. Cardinali, Time-dependency for the bimodal effect of melatonin on calcium uptake in rat hypothalamus, J. Neurol. Trans. 85 (1991) 1435–1463.

[98] K.R. Popper, Conjectures and Refutations: The Growth of Scientific Knowledge, Harper & Row, NY, 1963.

[99] J. Siemiatycki, Synthesizing the lifetime history of smoking, Cancer Epidemiol. Biomarkers Prev. 14 (2005) 2294–2295.

[100] M.J. Schoemaker, A.J. Swerdlow, A. Ahlbom, A. Auvinen, K.G. Blaasaas, E. Cardis, H.C. Christensen, M. Feychting, S.J. Hepworth, C. Johansen, L. Klaeboe, S. Lonn, P.A. McKinney, K. Muir, J. Raitanen, T. Salminen, J. Thomsen, T. Tynes, Mobile phone use and risk of acoustic neuroma: results of the Interphone case-control study in five North European countries, Brit. J. Cancer 93 (2005) 842–848.

[101] S. Sadetzki, A. Certrit, A. Jarus-Hakak, E. Cardis, Y. Deutch, S. Duvdevani, et al., Cellular phone use and risk of benign and malignant parotid gland tumors–a nationwide case-control study, Am. J. Epidemiol. 167 (4) (2008) 457–467

[102] A. Lahkola, A. Auvinen, J. Raitanen, M.J. Schoemaker, H.C. Christensen, M. Feychting, C. Johansen, L. Klaeboe, S. Lonn, A.J. Swerdlow, T. Tynes, T. Salminen, Mobile phone use and risk of glioma in 5 North European countries, Int. J. Cancer 120 (2007) 1769–1775.

[103] F. Oktem, F. Ozguner, H. Mollaoglu, A. Koyu, E. Uz, Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin, Arch. Med. Res. 36 (2005) 350–355.

[104] M. Yariktas, F. Doner, F. Ozguner, O. Gokalp, H. Dogru, N. Delibas, Nitric oxide level in the nasal and sinus mucosa after exposure to electromagnetic field, Otolaryngol. Head Neck Surg. 132 (2005) 713–716.

[105] F. Ozguner, Y. Bardak, S. Comlekci, Protectuve effects of melatonin and caffeic acid phenethyl ester against retinal oxidative stress in long-term use of mobile phone: a comparative study, Mol. Cell. Biochem. 282 (2006) 83–88.

[106] M. Porcelli, G. Cacciapuoti, S. Fusco, R. Massa, G. d'Ambrosio, C. Bertoldo, M. De Rosa, V. Zappia, Non-thermal effects of microwaves on proteins: thermophilic enzymes as model system, FEBS Lett. 402 (1997) 102–106.

[107] H. Bohr, J. Bohr, Microwave enhanced kinetics observed in ORD studies of a protein, Bioelectromagnetics 21 (2000) 68–72.

[108] F. Mancinelli, M. Caraglia, A. Abbruzzese, G. d'Ambrosio, R. Massa, E. Bismuto, Non-thermal effects of electromagnetic fields at mobile phone frequency on the refolding of an intracellular protein: myoglobin, J. Cell. Biochem. 93 (2004) 188–196.

[109] M. Caraglia, M. Marra, F. Mancinelli, G. d'Ambrosio, R. Massa, A. Giordano, A. Budillon, A. Abbruzzese, E. Bismuto, Electromagnetic fields at mobile phone frequency induce apoptosis and inactivation of the multi-chaperone complex in human epidermoid cancer cells, J. Cell. Biochem. 204 (2005) 539–548.

[110] F. Crick, What Mad Pursuit: A Personal View of Scientific Discovery, Basic Books, New York, 1988.

ELSEVIER

Pathophysiology 16 (2009) 89–102

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Genotoxic effects of radiofrequency electromagnetic fields

Hugo W. Ruediger *

Division of Occupational Medicine, Medical University of Vienna, Waehringer Guertel 18-20, Berggasse 4/33, 1090 Vienna, Austria

Received 24 October 2008; received in revised form 16 November 2008; accepted 16 November 2008

Abstract

101 publications are exploited which have studied genotoxicity of radiofrequency electromagnetic fields (RF-EMF) *in vivo* and *in vitro*. Of these 49 report a genotoxic effect and 42 do not. In addition, 8 studies failed to detect an influence on the genetic material, but showed that RF-EMF enhanced the genotoxic action of other chemical or physical agents. The controversial results may in part be explained by the different cellular systems. Moreover, inconsistencies may depend from the variety of analytical methods being used, which differ considerably with respect to sensitivity and specificity. Taking altogether there is ample evidence that RF-EMF can alter the genetic material of exposed cells *in vivo* and *in vitro* and in more than one way. This genotoxic action may be mediated by microthermal effects in cellular structures, formation of free radicals, or an interaction with DNA-repair mechanisms.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Gene mutations; Cytogenetic effects; DNA fragmentation; Mechanisms of genotoxicity

1. Introduction

Alterations of genetic information in somatic cells are the key event in the process of carcinogenesis [1,2]. Consequently any agent, which has a genotoxic attribute is suspected also to be cancerogenic. This is the driving force behind the multitude of studies on genotoxicity of radiofrequency electromagnetic fields (RF-EMF), conducted so far. A total of 101 publications on genotoxicity studies of RF-EMF are exploited here, of which 49 report genotoxic effects, subsequently marked as GT(+) (Table 1), 43 do not (Table 2), and 9 find, that RF-EMF do not induce genotoxic events by itself but enhance the genotoxic action of other physical or chemical agents (Table 3). Thus, in contrast to several reviews in the past [3–6], it now became evident that non-thermal genotoxic effects of RF-EMF is convincingly demonstrated by a substantial number of published studies. The studies have been performed with a variety of different test systems – some studies used more than one test system – which will be assigned here to the three principle endpoints of a genotoxic action: (1) effect on chromosomes, (2) DNA fragmentation, and (3) gene mutations.

* Tel.: +43 1 9582908.
E-mail address: hugo.ruediger@meduniwien.ac.at.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2008.11.004

2. Effect on chromosomes

This group comprises the analysis of numerical or structural anomalies of metaphase chromosomes (CA), sister-chromatid-exchanges (SCEs), and formation of micronuclei (MN). Of the 21 studies using CA, 9 are CA-positive, 11 CA-negative, and 1 reports an RF-induced enhancement of genotoxicity by X-rays. In general proliferating cells are required for the study of chromosomal effects, however, micronuclei have also been analysed in polychromatic erythrocytes and in exfoliated cells, for instance from buccal smears [7,8]. Moreover, aneuploidy rates of distinct chromosomes as well as chromosomal translocations can also be studied in interphase nuclei using fluorescence in situ hybridization (FISH). While structural aberrations detected by conventional CA are mainly lethal to the cell, translocations are persistent and may be passed to the cellular progeny. Using FISH increased levels of aneuploidy of chromosome 1, 10, 11, and 17 have been reported in human blood lymphocytes after RF-EMF exposure [9]. In metaphase chromosomes FISH may increase the sensitivity of chromosomal analysis [10] but this has only once been used for RF-EMF studies [11].

CA brings about to detect a variety of chromosomal aberrations. In contrast, micronuclei originate only from acentric

Table 1
Publications which report RF-EMF related genotoxic effects.

Reference	Biological system	Genotoxic endpoint	Results and comments
Aitken et al. [45]	Mouse sperm	QPCR and comet assay	Gel electrophoresis revealed no gross evidence of increased single- or double-DNA strand breakage in spermatozoa. However, a detailed analysis of DNA integrity using QPCR revealed damage to both the mitochondrial genome ($p<0.05$) and the nuclear-globin locus ($p<0.01$).
Balode [46]	Cow erythrocytes	Micronuclei (MN)	The counting of micronuclei in peripheral erythrocytes gave low average incidences, 0.6 per 1000 in the exposed group and 0.1 per 1000 in the control, but statistically significant ($p<0.01$) differences were found in the frequency distribution between the control and exposed groups.
Belyaev et al. [47]	Human blood lymphocytes	Chromatin condensation and 53BP1 foci	Decrease in background levels of 53BP1 foci and may indicate decrease in accessibility of 53BP1 to antibodies because of stress-induced chromatin condensation.
Busljeta et al. [48]	Rat hematopoietic tissues	MN	Erythrocyte count, haemoglobin and haematocrit were increased in peripheral blood (days 8 and 15). Concurrently, anuclear cells and erythropoietic precursor cells were decreased ($p<0.05$) in the bone marrow on day 15, but micronucleated cells' (MNCs) frequency was increased.
d'Ambrosio et al. [49]	Human blood lymphocytes	MN	The micronucleus frequency was not affected by CW exposure; however, a statistically significant micronucleus effect was found following exposure to phase modulated field.
Diem et al. [23]	Human cultured fibroblasts and rat granulosa cells	Alkaline and neutral comet assay	The intermittent exposure showed a stronger effect in the comet assay than continuous exposure.
Ferreira et al. [50]	Rat hematopoietic tissues exposed during embryogenesis	MN	The irradiated group showed a significant increase in MN occurrence.
Fucic et al. [15]	Human blood lymphocytes	MN	X-rays and microwaves were preferentially clastogens while vinyl chloride monomer showed aneugenic activity as well. Microwaves possess some mutagenic characteristics typical of chemical mutagens.
Gadhia et al. [51]	Human blood lymphocytes	Chromosomal aberrations and SCE	There was a significant increase ($p<0.05$) in dicentric chromosomes among mobile users who were smoker–alcoholic as compared to nonsmoker–nonalcoholic. Synergistic action with MMC, SCEs showed a significant increase among mobile users.
Gandhi and Singh [7]	Human blood lymphocytes and buccal mucosa cells	Chromosomal aberrations and MN	Increased number of micronucleated buccal cells and cytological abnormalities in cultured lymphocytes.
Gandhi, 2005 [52]	Human blood lymphocytes	Comet assay, *in vivo* capillary MN	Mean comet tail length (26.76 ± 0.054 mm; 39.75% of cells damaged) in mobile phone users was highly significant from that in the control group. The *in vivo* capillary blood MNT also revealed highly significant (0.25) frequency of micronucleated cells.
Garaj-Vrhovac et al [53]	Human blood lymphocytes	Chromosomal aberrations and MN	In all experimental conditions, the frequency of all types of chromosomal aberrations was significantly higher than in the control samples. In the irradiated samples the presence of dicentric and ring chromosomes was established. The incidence of micronuclei was also higher in the exposed samples.
Garaj-Vrhovac et al. [54]	Chinese hamster cells V79	DNA synthesis by [3H]thymidine uptake, and chromosomal aberrations	In comparison with the control samples there was a higher frequency of specific chromosome lesions in cells that had been irradiated.
Garaj-Vrhovac et al. [55]	Chinese hamster cells V79	Chromosomal aberrations and MN	Significantly higher frequency of specific chromosome aberrations such as dicentric and ring chromosomes in irradiated cells. The presence of micronuclei in irradiated cells confirmed the changes that had occurred in chromosome structure.
Garaj-Vrhovac et al. [56]	Human blood lymphocytes	MN	Increase in frequency of micronuclei as well as disturbances in the distribution of cells over the first, second and third mitotic division in exposed subjects compared to controls.
Haider et al. [57]	*Tradescantia* flower buds	MN	The results at all exposure sites except one were statistically significant.
Koyama et al. [12]	CHO-K1 cells	MN + kinetochore determination	RF at SAR of 78 W/kg and higher form MN with a particular increase of kinetochore-positive MN and potentiate MN formation induced by bleomycine treatment.
Lai et al. [58]	Rat brain cells	Comet assay	RFR exposure significantly increased DNA double strand breaks in brain cells of the rat, and the effect was partially blocked by treatment with naltrexone.
Lai and Singh [59]	Rat brain cells	Alkaline comet assay	No effects immediately after 2 h of exposure to pulsed microwaves, whereas a dose rate-dependent increase in DNA single strand breaks was found in brain cells of rats at 4 h post-exposure with CW and pulsed waves.

Lai and Singh [60]	Rat brain cells	Comet assay	Significantly higher levels of DNA single and double strand breaks. Exposure to 'noise' alone did not significantly affect the levels, however, simultaneous 'noise' exposure blocked microwave-induced increases in DNA strand breaks.
Lai and Singh [61]	Rat brain cells	Comet assay	An increase in DNA strand breaks was observed after exposure to either the pulsed or continuous-wave radiation, no significant difference was observed between the effects of the two forms of radiation.
Lai and Singh [35]	Rat brain cells	Comet assay	Treatment immediately before and after RFR exposure with either melatonin or *N*-tert-butyl-alpha-phenylnitrone (PBN) blocks induction of DSB by RFR. It is hypothesized that free radicals are involved in RFR-induced DNA damage in the brain cells of rats.
Lixia et al. [62]	Human lens epithelial cells	Comet assay and BudR incorporation	No DNA breaks at 1 and 2 W/kg but increase 0 and 30 min after exposure to 3 W/kg. Exposure at 2 and 3 W/kg for 2 h significantly increased HsP 70 protein but not mRNA expression.
Maes et al. [63]	Human blood lymphocytes	Chromosome aberrations	Some cytogenetic damage was obtained *in vitro* when blood samples were very close to the antenna. The questionable *in vivo* results (six maintenance workers) are not considered here.
Maes et al. [64]	Human blood lymphocytes	Chromosomal aberrations, SCE, and MN	Marked increase in the frequency of chromosome aberrations (including dicentric chromosomes and acentric fragments) and 19 micronuclei. On the other hand, the microwave exposure did not influence the cell kinetics nor the sister-chromatid-exchange (SCE) frequency.
Markova et al. [65]	Human blood lymphocytes	p53 binding protein and γH2AX foci	MWs from GSM mobile telephones affect chromatin conformation and 53BP1/gamma-H2AX foci similar to heat shock.
Mashevich et al. [66]	Human blood lymphocytes	Chromosomal aberrations	A linear increase in chromosome 17 aneuploidy was observed as a function of the SAR value.
Mazor et al. [9]	Human blood lymphocytes	Aneuploidy rate of Chr. # 1, 10, 11, 17 determined by interphase FISH	Increased levels of aneuploidy in chromosomes 1 and 10 at higher SAR, while for chromosomes 11 and 17 the increases were observed only for the lower SAR.
Nikolova et al. [67]	Mouse nestin-positive neural progenitor cells	Transcript of specific genes and proteins, proliferation, apoptosis, DNA DSB	Down-regulation of neural-specific Nurr1and up-regulation of bax and GADD45 mRNA levels. Short-term RF-EMF exposure for 6 h, but not for 48 h, resulted in a low and transient increase of DNA double strand breaks.
Paulraj and Behari [68]	Rat brain cells	Comet assay	Statistically significant ($p < 0.001$) increase in DNA single strand breaks in brain cells of rat.
Pavicic and Trosic [13]	V79 cells	Alteration of microtubule proteins	The microtubule structure altered after 3 h of irritation.
Phillips et al. [69]	Molt-4 T-lymphoblastoid cells	Comet assay	DNA damage decreased by (1) exposure to the iDEN signal (2.4 μW/g for 2 h or 21 h), (2) exposure to the TDMA signal (2.6 μW/g for 2 h and 21 h), (3) exposure to the TDMA signal (26 μW/g for 2 h), exposure to the iDEN signal (24 μW/g for 2 h) and 21 h significantly increased DNA damage.
Sarimov et al. [70]	Human blood lymphocytes	Chromatin condensation by anomalous viscosity	Analysis of pooled data from all donors showed statistically significant effect of 1-h exposure to MW. Effects differ at various GSM frequencies and vary between donors.
Sarkar et al. [71]	Mouse testis and brain cells	Restriction pattern after Hinfl treatment	As compared to control animals, band patterns in exposed animals were found to be distinctly altered in the range of 7–8 kb which was also substantiated by densitometric analysis.
Schwarz et al. [33]	Human cultured fibroblasts and lymphocytes	Alkaline comet assay and MN	UMTS exposure increased the CTF and induced centromere-negative micronuclei in human cultured fibroblasts in a dose- and time-dependent way. No UMTS effect was obtained with lymphocytes, either unstimulated or stimulated with phytohemagglutinin.
Sykes et al. [22]	pKZ1 mice	lacZ transgene inversion	No difference between the control and treated groups in the 1- and 5-day exposure groups, but a reduction in inversions below the spontaneous frequency in the 25-day exposure group. This suggests that RF radiation can lead to a perturbation in recombination frequency.
Tice et al. [72]	Human blood lymphocytes	Alkaline comet assay and MN	Exposure for either 3 or 24 h with the unmodulated signal did not induce a significant increase in DNA DSB or MN in lymphocytes. However, with the modulated signal there was a significant and reproducible increase in the frequency of micronucleated lymphocytes.
Tkalec et al. [14]	*Allium cepa* seeds	Germination, mitotic index, mitotic abnormalities	Increased mitotic aberrations in root meristematic cells of *A. cepa*. Effects were markedly dependent on the field frequencies applied as well as on field strength and modulation. Findings also indicate that mitotic effects of RF-EMF could be due to impairment of the mitotic spindle.
Trosic et al. [73]	Rat hematopoietic tissues	MN and polychromatic erythrocytes (PCEs)	The incidence of micronuclei/1000 PCEs in peripheral blood was significantly increased ($p < 0.05$) in the subgroup exposed to fro/MW radiation after eight irradiation treatments of 2 h each in comparison with the sham-exposed control group.

Table 1 (*Continued*)

Reference	Biological system	Genotoxic endpoint	Results and comments
Trosic et al. [74]	Rat hematopoietic tissues	MN and polychromatic erythrocytes	In polychromatic erythrocytes significant differences ($p<0.05$) for experimental days 8 and 15. The frequency of micronucleated PCEs was also significantly increased on experimental day 15 ($p<0.05$).
Trosic and Busljeta [75]	Rat hematopoietic tissues and peripheral blood	MN and polychromatic erythrocytes	BMPCEs were increased on days 8 and 15, and PBPCEs were elevated on days 2 and 8 ($p<0.05$).
Vijayalaxmi et al. [76]	C3H/HeJ cancer prone mice, peripheral blood and bone marrow	MN	No observed RF effects. A correction was published, stating that there was actually a significant MN increase in peripheral blood and bone marrow cells after chronic exposure to RF [Vijayalaxmi, M.R. Frei, S.J. Dusch, V. Guel, M.L. Meltz, J.R. Jauchem, Radiat. Res. 149 (3) (1998) 308].
Wu et al. [39]	Human epithelial lens cells	Comet assay and intracellular ROS	RF at 4 W/kg for 24 h significantly increased intracellular ROS and DNA damage. Both can be blocked completely by electromagnetic noise.
Yadav and Sharma [8]	Exfoliated buccal cells	MN in buccal cells	In exposed subjects 9.84 ± 0.745 micronucleated cells and 10.72 ± 0.889 total micronuclei (TMN) as compared to zero duration of exposure along with average 3.75 ± 0.774 MNC and 4.00 ± 0.808 TMN in controls. Correlation between 0–1, 1–2, 2–3 and 3–4 years of exposure and the frequency of MNC and TMN.
Yao et al. [40]	Human lens epithelial cells	Alkaline comet assay, gamma-H2AX foci, ROS level	SAR of 3 and 4 W/kg induced significant DNA damage in the comet assay, while no statistical difference in double strand breaks was found by γH2AX foci. Electromagnetic noise could block RF-induced ROS formation and DNA damage.
Yao et al. [41]	Human lens epithelial cells	Alkaline comet assay, γH2AX foci, ROS level	DNA damage was significantly increased by comet assay at 3 and 4 W/kg, whereas double strand breaks by γH2AX foci were significantly increased only at 4 W/kg. Significantly increased ROS levels were detected in the 3 and 4 W/kg groups.
Zhang et al. [77]	Chinese hamster lung cells (CHL)	γH2AX foci	Increased percentage of γH2AX foci positive cell of 1800 MHz RF EMF exposure for 24 h ($37.9 \pm 8.6\%$) or 2-acetylaminofluorene exposure ($50.9 \pm 9.4\%$). However, there was no significant difference between the sham-exposure and RF EMF exposure for 1 h ($31.8 \pm 8.7\%$).
Zotti-Martelli et al. [78]	Human blood lymphocytes	MN	Both spontaneous and induced MN frequencies varied in a highly significant way among donors ($p<0.009$) and between experiments ($p<0.002$), and a statistically significant increase of MN, although rather low, was observed dependent on exposure time ($p=0.0004$) and applied power density ($p=0.0166$).
Zotti-Martelli et al. [79]	Human blood lymphocytes	MN	The results showed for both radiation frequencies an induction of micronuclei as compared to the control cultures at a power density of 30 mW/cm^2 and after an exposure of 30 and 60 min.

Abbreviations: Mitomycin C (MMC), bleomycin (BLM), methylmethansulfonate (MMS), 4-nitroquinoline-1-oxide (4-NQ1O), ethylmethansulfonate (EMS), chromosomal aberration analysis (CA), micronucleus assay (MN), reactive oxygen species (ROS), and fluorescence *in vitro* hybridization (FISH).

Table 2
Publications which do not report RF-EMF related genotoxic effects.

Reference	Biological system	Genotoxic endpoint	Results and comments
Antonopouloset al. [80]	Human blood lymphocytes	SCE	No increase in SCE or cell cycle progression found.
Belyaev et al. [81]	Rat brain, spleen, and thymus	Comet assay	GSM MWs at 915 MHz did not induce PFGE-detectable DNA double stranded breaks or changes in chromatin conformation, but affected expression of genes in rat brain cells.
Bisht et al. [82]	Mouse C3H 10T cells	MN	CDMA (3.2 or 4.8 W/kg) or FDMA (3.2 or 5.1 W/kg) RF-EMF radiation for 3, 8, 16 or 24 h did not result in a significant increase either in the percentage of binucleated cells with micronuclei or in the number of micronuclei per 100 binucleated cells.
Chang et al. [83]	*Escherichia coli* tester strain	Bacterial mutagenicity (Ames test)	No mutagenic or co-mutagenic effect with 4-NQ1O.
Ciaravino et al. [84]	CHO cells	SCE	Radiofrequency electromagnetic radiation (RF-EMF) did not change the number of SCEs that were induced by adriamycin.
Garson et al. [85]	Human blood lymphocytes	CA	No RF-EMF effect observed.
Gorlitz et al. [86]	B6C3F1 mice lymphocytes, erythrocytes, and keratinocytes	MN	No visible effect.
Gos et al. [87]	*Saccharomyces cerevisiae*	Mutation rates	No effects in fluctuation tests on forward mutation rates at CAN1, on the frequency of petite formation, on rates of intra-chromosomal deletion formation, or on rates of intra-genic recombination in the absence or presence of MMS.
Hook et al. [88]	Molt-4 T lymphoblastoid cells	Comet assay	No RF-EMF effects observed.
Juutilainen et al. [89]	Female CBA/S mice and K2 female transgenic mice	MN in erythrocytes	No effect on MN frequency.
Kerbacher et al. [90]	CHO cells	CA	No alteration was observed in the extent of chromosome aberrations induced by either simultaneous fro radiation exposure or convection heating to equivalent temperatures.
Komatsubara et al. [91]	Mouse m5S cells	CA	No effect on CA; temperature increase up to 41 °C at 100 W/kg.
Koyama et al. [92]	CHO cells	MN	No MN increase in cells exposed to HFEMF at a SAR of lower than 50 W/kg, while those at SARs of 100 and 200 W/kg were significantly higher when compared with the sham-exposed controls (temperature effect).
Lagroye et al. [93]	Rat brain cells	Alkaline comet assay	No observed effect.
Lagroye et al. [94]	C3H 10T1/2 cells	Comet assay, DNA–protein crosslinks	No observed effect.
Li et al. [95]	Murine C3H 10T cells	Comet assay	No observed effect.
Maes et al. [96]	Human blood lymphocytes	CA, SCE	Combined exposure of RF-EMF and to MMC and X-rays. Overall, no indication was found of a mutagenic, and/or co-mutagenic/synergistic effect.
Maes et al. [97]	Human blood lymphocytes	CA, SCE	Combined treatments with X-rays or MMC did not provide any indication of a synergistic action between the RF-EMF fields and X-rays or MMC.
Maes et al. [98]	Human blood lymphocytes	CA, SCE, Comet assay	The alkaline comet assay, SCE, and CA tests revealed no evidence of RF-EMF-induced genetic effects. No cooperative action was found between the electromagnetic field exposure and MMC using either the comet assay or SCE test.
Malyapa et al. [99]	Rat brain cells	Comet assay	No significant differences observed.
Malyapa et al. [100]	U87MG and C3H 10T1/2 cells	Comet assay	No significant differences observed.
Malyapa et al. [101]	U87MG and C3H 10T1/2 cells	Comet assay	No significant differences observed.
McNamee et al. [102]	Human blood lymphocytes	Comet assay and MN	No significant differences observed.
McNamee et al. [103]	Human blood lymphocytes	Comet assay and MN	No significant differences observed.
McNamee et al. [104]	Human blood lymphocytes	Comet assay	No significant differences observed.
Meltz et al. [105]	L5178Y mouse leukemic cells	Mutation in TK locus	No effect of RF-EMF alone or in the induced mutant frequency due to the simultaneous exposure to RF-EMF and proclaim, as compared with the proflavin exposures alone.
Ono et al. [106]	lacZ-transgenic mice	Mutations at the lac gene in spleen, liver, brain and testis	Mutation frequencies at the lacZ gene in spleen, liver, brain, and testis were similar to those observed in non-exposed mice.

Table 2 (*Continued*)

Reference	Biological system	Genotoxic endpoint	Results and comments
Roti Roti et al. [107]	C3H 10T1/2 cells	Transformed foci	No statistically significant differences observed.
Sakuma et al. [108]	Human glioblastoma A172 cells and fetal lung fibroblasts	DNA strand breaks (comet assay?)	No statistically significant differences.
Scarfi et al. [109]	Human blood lymphocytes	MN	No statistically significant differences observed.
Speit et al. [24]	Human cultured fibroblasts	Comet assay and MN	No statistically significant differences observed.
Stronati et al. [110]	Human blood lymphocytes	Comet assay, CA, SCE, MN	By comparison with appropriate sham-exposed and control samples, no effect of RF-EMF alone could be found for any of the assay endpoints. In addition RF-EMF did not modify any measured effects of the X-radiation.
Takahashi et al. [111]	Big Blue mice brain tissues	lacZ transgene inversion	No statistically significant differences observed.
Verschaeve et al. [112]	Rat brain and liver tissues, erythrocytes	MN (erythrocytes) and comet assay	No genotoxic effect of RF-EMF alone. Co-exposures to MX and RF-EMF radiation did not significantly increase the response of blood, liver and brain cells compared to MX exposure only.
Vijayalaxmi et al. [113]	Human blood lymphocytes	CA and MN	No observed RF-EMF effects.
Vijayalaxmi et al. [114]	Human blood lymphocytes	CA and MN	No observed RF-EMF effects.
Vijayalaxmi et al. [115]	Human blood lymphocytes	Comet assay	No observed RF-EMF effects.
Vijayalaxmi et al. [116]	Human blood lymphocytes	CA, MN	No observed RF-EMF effects.
Vijayalaxmi et al. [117]	Rat hematopoietic tissues and erythrocytes	MN	No observed RF-EMF effects.
Vijayalaxmi et al. [118]	Rat whole body and head only exposures. BM erythrocytes	MN	No observed RF-EMF effects.
Vijayalaxmi et al. [119]	CF-1 male mice, peripheral blood and bone marrow	MN	No observed RF-EMF effects.
Zeni et al. [120]	Human blood lymphocytes	Comet assay, CA, SCE	No observed RF-EMF effects.
Zeni et al. [121]	Human blood lymphocytes	MN	No observed RF-EMF effects.

Abbreviations: Chromosomal aberration analysis (CA), methotrexat (MX), mitomycin C (MMC), 4-nitroqinoline-1-oxide (4-NQ1O), methylmethansulfonate (MMS), code division multiple access (CDMA), frequency division multiple access (FDMA), and time division multiple access (TDMA).

Table 3
Publications which report synergistic RF-EMF effects in combination with other genotoxicants.

Reference	Genotoxic agents	Biological system	Genotoxic endpoint	Results and comments
Baohong et al. [122]	MMC, BLM, MMS, 4-NQ1O	Human blood lymphocytes	Alkaline comet assay	1.8 GHz RFR (SAR, 3 W/kg) for 2 h did not induce DSB, but could enhance the human lymphocyte DNA damage effects induced by MMC and 4-NQ1O. The synergistic DNA damage effects with BLM or MMS were not obvious.
Baohong et al. [123]	254 nm UVC	Human blood lymphocytes	Alkaline comet assay	RF exposure for 1.5 and 4 h did not enhance significantly human lymphocyte DNA damage, but could reduce and increase DNA damage of human lymphocytes induced by UVC at 1.5 and 4 h incubation respectively.
Kim et al. [124]	Cyclophosphamide, 4-NQ1O, EMS	L5178Y mouse lymphoma cells (comet assay) and CHL cells (CA)	Alkaline comet assay and CA	No direct cytogenetic effect of RF alone or in combination with cyclophosphamide or 4-NQ1O was found in the CA test and in the comet assay. However, RF had a potentiating effect in combination with cyclophosphamide or 4-NQ1O.
Maes et al. [125]	MMC	Human blood lymphocytes	SCE	Synergistic effect was observed with MMC.
Maes et al. [126]	MMC	Human blood lymphocytes	CA, SCE, comet assay	The combined exposure of the cells to the radiofrequency fields followed by their cultivation in the presence of mitomycin C revealed a very weak effect when compared to cells exposed to mitomycin C alone.
Manti et al. [11]	Previous 4 Gy X-ray radiation	Human blood lymphocytes	Chromosome aberration by FISH	No significant variations due to the UMTS exposure in the fraction of aberrant cells, but frequency of exchanges per cell in X-ray irradiated cells was significantly increased by UMTS at 2 W/kg.
Wang et al. [127]	254 nm UVC	Human blood lymphocytes	Comet assay	RF did not induce DNA damage but reduced or enhanced DNA damage by UVC at 1.5 or 4.0 h respectively.
Wang et al. [128]	MMC, BLM, MMS, 4-NQ1O	Human blood lymphocytes	Comet assay	RF did not induce DNA damage but enhanced DNA damage induced by MMC and 4-NQ1O.
Zhang et al. [129]	MMC	Human blood lymphocytes	Comet assay, micronucleus assay	No RF-induced DNA and chromosome damage, but increased MMC DNA damage by RF in comet assay.

Abbreviations: Mitomycin C (MMC), bleomycin (BLM), methylmethansulfonate (MMS), 4-nitroquinoline-1-oxide (4-NQ1O), ethylmethansulfonate (EMS), chromosomal aberration analysis (CA), fluorescence *in vitro* hybridization (FISH).

fragments of chromosomes or from lagged chromosomes secondary to mitotic non-disjunction, the latter being detected by indirect immunofluorescence using kinetochore antibodies. Kinetochore-positive MN arise by epigenetic mechanisms (disturbances of the spindle apparatus). Kinetochore-negative MN arise from acentric chromosomal fragments. This is an important distinction, but has been performed in a few RF-EMF studies only, of which only one [12] reports an increase of kinetochore-positive MN albeit after a high SAR $\geq$ 78 W/kg. Two studies describe RF-EMF-induced disturbances of the spindle apparatus [13,14], and one reports an aneugenic RF-EMF effect on the basis of the size distribution of MN [15]. Of a total of 39 studies using the micronucleus assay 22 are MN-positive, and 17 MN-negative.

SCEs are analysed in metaphase chromosomes after two rounds of replication in the presence of 5-bromodeoxyuridine (BUDR). SCEs, which are induced during the S-phase of the cell cycle, represent an exchange between homologous chromatids, an event which by itself is genetically neutral. Nevertheless it is considered to reflect a recombinational repair of DNA double strand breaks (DSB), and may therefore serve as an indicator of genotoxic stress. Of 10 studies using SCE a GT(+) effect was reported in one only, 8 were negative, and one study reports RF-induced enhancement of genotoxicity by mitomycin C.

3. DNA fragmentation

The comet assay, also known as a "Single Cell Gel electrophoresis assay" (SCG), and the detection of gamma-H2AX foci are the most frequently used techniques to study RF-EMF-induced DNA strand breaks. The comet assay uses interphase nuclear DNA, which is unwinded under alkaline conditions and subsequently subjected to an electric field. Here DNA fragments migrate towards the anode, thereby forming a comet-like tail [16,17]. The alkaline comet assay detects DNA single strand as well as double strand breaks, but is not applicable in the presence of DNA crosslinking agents [18]. These breaks may occur not only by toxic influences but also by transcriptional and repair processes and by alkali-sensitive sites. Therefore this frequently used and very sensitive assay has a poor specificity. Of 41 studies using the comet assay 15 report comet-positive and 19 comet-negative results after RF-EMF exposure. RF-EMF enhancement of comet assay effects caused by other genotoxic agents is described in 7 studies.

Out of a multitude of DNA damage checkpoint proteins two have been used to detect DBS: H2AX, a member of the nuclear histone family [19], and P53 binding protein (53BP1). Both are rapidly phosphorylated only minutes after DNA damage and are then gathered in the vicinity of DNA double strand breaks. Here they form foci which can be visualized by indirect immunofluorescence [20,21]. These foci represent an initial and specific step in the repair process of exogenously induced DNA double strand breaks. It is important to realize, however, that repair processes of DSB are quantified, not DSB themselves. The method has been employed in 4 studies, predominantly using the yH2AX foci test. In all instances GT(+) effects have been detected.

DNA alterations have also been analysed by the anomalous viscosity time dependency test (AVTD, 1 GT(+) study), detecting conformational changes, and by quantitative PCR (QPCR, 1 GT(+) study) detecting structural changes in the DNA.

4. Gene mutations

In this category 6 studies have been performed using 4 different endpoints: (1) Altered restriction fragments (1 GT(+) study), (2) lacZ inversion in transgenic mice. This method has been used in 3 studies which all failed to detect an increased rate of inversions, but one found a reduced rate as compared to unexposed controls [22], which is interpreted as a RF-EMF-induced reduction of recombination repair. (3) Mutation at the thymidine kinase (TK) locus (1 negative study). (4) Bacterial his$^-$ revertants (Ames test, 1 negative study).

5. Discussion

The large number of contradictory results among the 101 published studies on a genotoxic action of RF-EMF is tangling. Nevertheless patterns can be perceived. GT(+) as well as GT(−) findings have been reported at a standard absorption ratio (SAR) below 0.05 up to 100 W/kg and an exposure of 15 min and 48 h *in vitro*, and between hours and years *in vivo*. The outcome of studies was nearly independent from RF frequencies between 300 and 7700 MHz and the type of RF signal, either continuous wave (CW) or pulse-modulated (PM). GT(+) was obtained in 15 CW and 26 PM exposures, GT(−) in 14 CW and 27 PM exposures (some studies did not indicate the type of signal used). Contradictory results have been obtained even when two experienced groups performed the same experiments using the same cells and identical exposure conditions [23,24]. This may reflect a general problem of genotoxic studies being dependent on a multitude of factors which are difficult to control [25]. Some of the studies exploited here have shortcomings with respect to incompletely described or unreliable exposure conditions and/or an inadequate experimental design. Even a considerable publication bias in favour of negative results has been suspected (www.microwavenews.com/RR.html, 2006) [26].

The proportion of GT(+) effects is much higher *in vivo* (23/40) than *in vitro* (29/77). (Since some studies have been performed on more than one biological system, the total number of GT(+) and GT(−) effects exceeds the total number of published studies.) Considering all genotoxic endpoints applied, the frequently used parameters chromosome analysis (9/21 GT(+)), comet assay (15/41 GT(+)), and sister-chromatid-exchange (1/10 GT(+)) showed the highest

proportion of negative results, while the micronucleus assay yielded more positive than negative results (22/39 GT(+)). Since the SCE test which was negative in nearly all cases is known to be rather insensitive to radiomimetic (clastogenic) agents it can be speculated, that a clastogenic mechanism is involved in RF-EMF genotoxic action.

Epigenetic influences may also contribute to genotoxicity as demonstrated by RF-EMF-induced chromosomal non-disjunction and disturbances of the mitotic spindle. This is in agreement with the higher proportion of 22/39 GT(+) findings among studies using the micronucleus assay as compared to those using CA, because some of the micronuclei may represent lagged chromosomes. Epigenetic mechanisms may also be effective after a combined exposure to RF-EMF and various physical or chemical mutagens (Table 4). RF-EMF preferentially enhanced the genotoxic effect of 4-NQ1O (4/4), MMC (4/8), UVC (2/2), and cyclophosphamide (2/2). No synergistic effect was obtained using MMS and EMS (3/3), BLM (2/2), and adriamycine (2/2). Only one out of 3 studies reported a synergistic effect with X-rays.

Cells and tissues of different origin exhibit a clearly variable sensitivity for genotoxic RF-EMF effects (Table 4). This has also been observed with extremely low frequency (ELF)-EMF [27] and may be dependent on genetic differences [28]. GT(+) effects of RF-EMF were reported predominantly in the following biological systems: human lens epithelial cells (4/4), human buccal mucosa cells (2/2), rodent brain tissues (8/13), and rat hemopoietic tissues (5/7). GT(−) results have been obtained with mouse permanent cell lines (7/7) and permanent lymphoblastoid cells of various origin (7/7). This is in a striking analogy to RF-EMF-induced reduction of ornithine decarboxylase activity being detected in primary but not in secondary neural cells [29].

6. Proposed mechanisms of RF-EMF genotoxicity

Cells are unusually sensitive to electromagnetic fields [30]. Weak fields may accelerate electron transfer and thereby destabilize the H-bond of cellular macromolecules. This could explain the stimulation of transcription and protein expression, which has been observed after RF-EMF exposure [31,32]. However, the energy of weak EM fields is not sufficient directly to break a chemical bond in DNA. Therefore it can be concluded, that genotoxic effects are mediated by indirect mechanisms as microthermal processes, generation of oxygen radicals (ROS), or a disturbance of DNA-repair processes.

6.1. Thermal effects

An increase of temperature in the culture medium of RF-EMF exposed cells has been observed at very high SAR levels only [12]. The vast majority of GT(+) studies were conducted at SAR < 2.0 not leading to a detectable increase of temperature in the culture medium. Moreover, similar or larger effects have been observed at a 5′ on/10′ off intermittent exposure [23,33], a result that contradicts a

Table 4
Distribution RF-EMF effects in 101 published studies.

Biological system	RF-EMF effects		Synergistic effects	
	Positive	Negative	Positive	Negative
In vitro (all cells and tissues)	29	39	9	11
Human blood lymphocytes	18	23	8	4
Human lens epithelial cells	4			
Human cultured fibroblasts	2	2		
Human glioblastoma cells		3		
Human lymphoblastoid cells		2		
Mouse permanent cell lines		6		1
Mouse lymphoblastoid cells		1	1	1
Chinese hamster cells (CHO, V79)	4	2		3
E. coli		1		2
Yeast		1		
Rat granulosa cells	1			
In vivo (all species and tissues)	23	17	0	1
Human blood lymphocytes	4	2		
Human buccal mucosa cells	2			
Mouse sperm	1			
Mouse brain tissues	2			
Mouse polychromatic erythrocytes		4		
Rat brain tissues	6	4		1
Rat hemopoietic tissues	5	2		
Rat spleen, liver		2		
lacZ-transgenic mice		3		
Plants	2			
Cattle polychromatic erythrocytes	1			

Since several published studies have used more than 1 biological system the total of negative and positive effects exceeds the number of 101 publications.

simple temperature-based mechanism of the observed genotoxic action. However, experimental results with microwave absorption at colloidal interfaces have demonstrated that the electric absorption of microwaves between 10 and 4000 MHz goes through a maximum with the size of bride droplets >100 and <10,000 nm, and depends on the type of ions and their concentrations [34]. This local absorption of microwaves may therefore lead to a considerable local heating in living cells during low energy microwave exposure.

6.2. Oxygen radicals

There is evidence that RF-EMF may stimulate the formation of reactive oxygen species in exposed cells *in vivo* [35–37] and *in vitro* [38–41]. Free oxygen radicals may form base adducts in DNA, the most important lesion being 8-OHdG, and oxidize also other cellular components, such as lipids leaving behind reactive species, that in turn can couple to DNA bases [42]. The first step in the generation of ROS by microwaves is mediated in the plasma membrane by NADH oxidase [43]. Subsequently ROS activates matrix metalloproteases (MMP), thereby initiating intracellular signalling cascades. It is interesting to note that these processes start within 5 min of radiation and at a very low field intensity of 0.005 W/cm^2. Moreover, higher effects have been obtained by intermittent radiation, when cells were left unirradiated for 10 min. This is in agreement with *in vitro* genotoxicity studies using the comet assay [23,33].

6.3. Alteration of DNA-repair processes

A considerable proportion of studies have investigated the consequences of a combined exposure to RF-EMF and various chemical or physical mutagens. 8/12 studies using human blood lymphocytes have demonstrated that RF-EMF enhanced the genotoxic action of other agents, preferentially of UV, MMC, or 4-NQ1O (an UV-mimetic agent). Since in all these experiments microwave exposure failed to induce detectable genotoxic effect by itself, an interference with DNA-repair mechanisms has been postulated, however, there is no direct experimental proof yet. An alteration of recombinational repair has also been proposed by Sykes et al. [22] as an explanation of the reduced rate of inversions in lacZ-transgenic mice after RF-EMF treatment.

An influence of microwave exposure on DNA-repair processes has long been proposed for power frequency electromagnetic fields [35]. A recent epidemiological investigation into the frequency of polymorphisms of DNA-repair genes in children with acute leukemia living in the vicinity of power line transformers [44] emphasizes the significance DNA-repair impairment for an EMF related increase of this malignancy. There was a significant gene–environment interaction (COR = 4.31) between the electromagnetic field intensities and a less active genetic variant of XRCC1, a crucial enzyme in base excision repair.

References

[1] B.N. Ames, W.E. Durston, E. Yamasaki, F.D. Lee, Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection, Proc. Natl. Acad. Sci. U.S.A. 70 (1973) 2281–2285.

[2] W.F. Bodmer, Cancer genetics, Br. Med. Bull. 50 (1994) 517–526.

[3] L. Verschaeve, A. Maes, Genetic, cancerogenic and teratotogenic effects of radiofrequency fields, Mutat. Res. 410 (1998) 141–165.

[4] M.L. Meltz, Radiofrequency exposure and mammalian cell toxicity, genotoxicity, and transformation, Bioelectromagnetics (Suppl. 6) (2003) S196–S213.

[5] Vijayalaxmi, G. Obe, Controversial cytogenetic observations in mammalian somatic cells exposed to radiofrequency radiation, Radiat. Res. 162 (2004) 481–496.

[6] L. Verschaeve, Genetic effects of radiofrequency radiation (RFR), Toxicol. Appl. Pharmacol. 2007 (2005) S336–S341.

[7] G. Gandhi, P. Singh, Cytogenetic damage in mobile phone users: preliminary data, Int. J. Hum. Genet. 5 (4) (2005) 259–265.

[8] O. Yadav, M.K. Sharma, Increased frequency of micronucleated exfoliated cells among humans exposed in vivo to mobile telephone radiations, Mutat. Res. 650 (2008) 175–180.

[9] R. Mazor, A. Korenstein-Ilan, A. Barbul, Y. Eshet, A. Sahadi, E. Jerby, Korenstein, Increased levels of numerical chromosome aberrations after in vitro exposure of human peripheral blood lymphocytes to radiafrequency electromagnetic fields for 72 hours, Radiat. Res 169 (2008) 28–37.

[10] M.R. Speicher, N.P. Carter, The new cytogenetics: Blurring the boundaries with molecular biology, Nature Rev. Genet. 6 (2005) 782–792.

[11] L. Manti, H. Braselmann, M.L. Calabrese, R. Massa, M. Pugliese, P. Scampoli, G. Sicignano, G. Grossi, Effects of modulated microwave radiation at cellular telephone frequency (1.95 GHz) on X-ray-induced chromosome aberrations in human lymphocytes in vitro, Radiat. Res. 169 (2008) 575–583.

[12] S. Koyama, T. Nakahara, K. Wake, M. Taki, Y. Isozumi, J. Miyakoshi, Effects of high frequency electromagnetic fields on micronucleus formation inCHO-K1 cells, Mutat. Res. 541 (2003) 81–89.

[13] I. Pavicic, I. Trosic, In vitro testing of cellular response to ultra high frequency electromagnetic field radiation, Toxicol. In Vitro 22 (2008) 1344–1348.

[14] M. Tkalec, K. Malaric, M. Pavlica, B. Pevalek-Kozlina, Z. Vidakovic-Cifrek, Effects of radiofrequency electromagnetic fields on seed germination and root meristematic cells of *Allium cepa* L., Mutat. Res. (2008), doi:10.1016/j.mrgentox.2008.09.022.

[15] A. Fucic, V. Garaj-Vrhovac, M. Skara, B. Dimitrovic, X-rays, microwaves and vinyl chloride monomer: their clastogenic and aneugenic activity, using the micronucleus assay on human lymphocytes, Mutat. Res. 282 (4) (1992) 265–271.

[16] O. Ostling, K.J. Johanson, Microelectrophoretic study of radiation-induced DNA damages in individual mammalian cells, Biochem. Biophys. Res. Commun. 123 (1984) 291–298.

[17] N.P. Singh, M.T. McCoy, R.R. Tice, E.L. Schneider, A simple technique for quantitation of low levels of DNA damage in individual cells, Exp. Cell Res. 175 (1988) 184–191.

[18] G. Speit, M. Fröhler-Keller, P. Schütz, S. Neuss, Low sensitivity of the comet assay to detect acetaldehyde-induced genotoxicity, Mutat. Res. 657 (2008) 93–97.

[19] T.T. Paull, E.P. Rogakou, V. Yamazaki, C.U. Kirchgessner, M. Gellert, W.M. Bonner, A critical role for histone H2AX in recruitment of repair factors to nuclear foci after DNA damage, Curr. Biol. 10 (2000) 886–895.

[20] O. Fernandez-Capetillo, H.A.T. Chen, A. Celeste, I. Ward, P.J. Romanienko, J.C. Morales, K. Naka, Z. Xia, D. Camerini-Otero, N. Motoyama, P.B. Carpenter, W.M. Bonner, J. Chen, A. Nussenzweig, DNA damage-induced G2-M checkpoint activation by histone H2AX and 53BP1, Nat. Cell Biol. 4 (2002) 993–997.

[21] O. Fernandez-Capetillo, A. Lee, M. Nussenzweig, A. Nussenzweig, H2AX: the histone guardian of the genome, DNA Repair 3 (2004) 959–967.

[22] P.J. Sykes, B.D. McCallum, M.J. Bangay, A.M. Hooker, A.A. Morley, Effect of exposure to 900 MHz radiofrequency radiation on intrachromosomal recombination in pKZ1 mice, Radiat. Res. 156 (5) (2001) 495–502.

[23] E. Diem, C. Schwarz, F. Adlkofer, O. Jahn, H.W. Ruediger, Non-thermal DNA breakage by mobile-phone radiation (1800 MHz) in human fibroblasts and in transformed GFSH-R17 rat granulosa cells in vitro, Mutat. Res. 583 (2005) 178–183.

[24] G. Speit, P. Schuetz, H. Hoffmann, Genotoxic effects of exposure to radiofrequency electromagnetic fields (RF-EMF) in cultured mammalian cells are not independently reproducible, Mutat. Res. 626 (2007) 42–47.

[25] D. Blakey, S.M. Galloway, D.J. Kirkland, J.T. MacGregor, Regulatory aspects of genotoxicity testing: from hazard identification to risk assessment, Mutat. Res. 657 (2008) 84–90.

[26] A. Huss, M. Egger, K. Hug, K. Huwiler-Müntener, M. Röösli, Source of funding and results of studies of health effects of mobile phone use: systematic review of experimental studies, Environ. Health. Perspect. 115 (2007) 1–4.

[27] S. Ivancsits, A. Pilger, E. Diem, O. Jahn, H.W. Rüdiger, Cell type-specific genotoxic effects of intermittent extremely low-frequency electromagnetic fields, Mutat. Res. 583 (2005) 184–188.

[28] A.L. Di Carlo, T.A. Litovitz, Is genetics the unrecognized confounding factor in bioelectromagnetics? Flock-dependence of field-induced anoxia protection in chick embryos, Bioelectrochem. Bioelectromagn. 48 (1999) 209–215.

[29] A. Höytö, J. Juutilainen, J. Naarala, Ornithine decarboxylase activity is affected in primary astrocytes but not in secondary cell lines exposed to 872 MHz RF radiation, Int. J. Radiat. Biol. 83 (6) (2007) 367–374.

[30] M. Blank, R. Goodman, Initial interactions in electromagnetic field-induced biosynthesis, J. Cell. Physiol. 199 (2004) 359–363.

[31] S. Lee, D. Johnson, K. Dunbar, H. Dong, X. Ge, Y.C. Kim, C. Wing, N. Jayathilaka, N. Emmanuel, C.Q. Zhou, H.L. Gerber, C.C. Tseng, S.M. Wang, 2.45 GHz radiofrequency fields alter gene expression in cultured human cells, FEBS Lett. 579 (21) (2005) 4829–4836.

[32] R. Nylund, D. Leszczynski, Mobile phone radiation causes changes in gene and protein expression in human endothelial cell lines and the response seems to be genome- and proteome-dependent, Proteomics 17 (2006) 4769–4780.

[33] C. Schwarz, E. Kratochvil, A. Pilger, N. Kuster, F. Adlkofer, H.W. Ruediger, Radiofrequency electromagnetic fields (UMTS, 1,950 MHz) induce genotoxic effects in vitro in human fibroblasts but not in lymphocytes, Int. Arch. Occup. Environ. Health 81 (2008) 755–767.

[34] C. Holtze, R. Sivaramakrishnan, M. Antonietti, J. Tsuwi, F. Kremer, K.D. Kramer, The microwave absorption of emulsions containing aqueous micro- and nanodroplets: a means to optimize microwave heating, J. Colloid Interf. Sci. 302 (2) (2006) 651–657.

[35] H. Lai, N.P. Singh, Melatonin and a spin-trap compound block radiofrequency electromagnetic radiation-induced DNA strand breaks in rat brain cells, Bioelectromagnetics 18 (6) (1997) 446–454.

[36] F. Oktem, F. Ozguner, H. Mollaoglu, A. Koyu, E. Zu, Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin, Arch. Med. Res. 36 (4) (2005) 350–355.

[37] M. Tkalec, K. Malaric, B. Pevalek-Kozlina, Exposure to radiofrequency radiation induces oxidative stress in duckweed *Lemna minor* L., Sci. Total Environ. 388 (1–3) (2007) 78–89.

[38] M. Zmyslony, P. Politanski, E. Rajkowska, W. Szymczak, J. Jajte, Acute exposure to 930 MHz CW electromagnetic radiation in vitro affects reactive oxygen species level in rat lymphocytes treated by iron ions, Bioelectromagnetics 25 (2004) 324–328.

[39] W. Wu, K. Yao, K.J. Wang, D.Q. Lu, J.L. He, L.H. Xu, W.J. Sun, Blocking 1800 MHz mobile phone radiation-induced reactive oxygen species production and DNA damage in lens epithelial cells by noise magnetic fields, Zhejiang Da Xue Xue Bao Yi Xue Ban 37 (2008) 34–38 (Chinese languange).

[40] K. Yao, W. Wu, K. Wang, S. Ni, P. Ye, Y. Ye, J. Ye, L. Sun, Electromagnetic noise inhibits radiofrequency radiation-induced DNA damage and reactive oxygen species increase in human lens epithelial cells, Mol. Vis. 19 (2008) 964–969.

[41] K. Yao, W. Wu, Y. Yu, Q. Zeng, J. He, D. Lu, K. Wang, Effect of superposed electromagnetic noise on lens epithelial cells induced by microwave radiation, Invest. Ophthalmol. Vis. Sci. 49 (2008) 2009–2015.

[42] M. Valko, M. Izakovic, M. Mazur, C.J. Rhodes, J. Telser, Role of oxygen radicals in DNA damage and cancer incidence, Mol. Cell. Biochem. 266 (2004) 37–56.

[43] J. Friedman, S. Kraus, Y. Hauptman, Y. Schiff, R. Seger, Mechanisms of short-term ERK activation by electromagnetic fields at mobile phone frequencies, Biochem. J. 405 (2007) 559–568.

[44] Y. Yang, J. Xingming, Y. Chonghuai, T. Ying, T. Jingyan, S. Xiaoming, Case-only study of interactions between DNA repair genes (hMLH1, APEX1, MGMT, XRCC1 and XPD) and low-frequency electromagnetic fields in childhood acute leukemia, Leuk. Lymphoma 49 (12) (2008) 2344–2350.

[45] R.J. Aitken, L.E. Bennetts, D. Sawyer, A.M. Wiklendt, B.V. King, Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline, Int. J. Androl. 28 (2005) 171–179.

[46] Z. Balode, Assessment of radio-frequency electromagnetic radiation by the micronucleus test in bovine peripheral erythrocytes, Sci. Total Environ. 180 (1) (1996) 81–85.

[47] I.Y. Belyaev, L. Hillert, M. Protopopova, C. Tamm, L.O. Malmgren, B.R. Persson, G. Selivanova, M. Harms-Ringdahl, 915 MHz microwaves and 50 Hz magnetic field affect chromatin conformation and 53BP1 foci in human lymphocytes from hypersensitive and healthy persons, Bioelectromagnetics 26 (3) (2005) 173–184.

[48] I. Busljeta, I. Trosic, S. Milkovic-Kraus, Erythropoietic changes in rats after 2.45 GJz nonthermal irradiation, Int. J. Hyg. Environ. Health 207 (6) (2004) 549–554.

[49] G. d'Ambrosio, R. Massa, M.R. Scarfi, O. Zeni, Cytogenetic damage in human lymphocytes following GMSK phase modulated microwave exposure, Bioelectromagnetics 23 (2002) 7–13.

[50] A.R. Ferreira, T. Knakievicz, M.A. Pasquali, D.P. Gelain, F. Dal-Pizzol, C.E. Fernandez, A.A. DeSalles, H.B. Ferreira, J.C. Moreira, Ultra high frequency-electromagnetic field irradiation during pregnancy leads to an increase in erythrocytes micronuclei incidence in rat offspring, Life Sci. 80 (2006) 43–50.

[51] P.K. Gadhia, T. Shah, A. Mistry, M. Pithawala, D. Tamakuwala, A preliminary study to assess possible chromosomal damage among users of digital mobile phones, Electromagn. Biol. Med. 22 (2–3) (2003) 149–159.

[52] G.A. Gandhi, Genetic damage in mobile phone users: some preliminary findings, Indian Hum. Genet. 11 (2) (2005) 99–104.

[53] V. Garaj-Vrhovac, A. Fucic, D. Horvat, The correlation between the frequency of micronuclei and specific chromosome aberrations in human lymphocytes exposed to microwave radiation in vitro, Mutat. Res. 281 (3) (1992) 181–186.

[54] V. Garaj-Vrhovac, D. Horvat, Z. Koren, The effect of microwave radiation on the cell genome, Mutat. Res. 243 (2) (1990) 87–93.

[55] V. Garaj-Vrhovac, D. Horvat, Z. Koren, The relationship between colony-forming ability, chromosome aberrations and incidence of micronuclei in V79 Chinese hamster cells exposed to microwave radiation, Mutat. Res. 263 (3) (1991) 143–149.

[56] V. Garaj-Vrhovac, Micronucleus assay and lymphocyte mitotic activity in risk assessment of occupational exposure to microwave radiation, Chemosphere 39 (13) (1999) 2301–2312.

[57] T. Haider, S. Knasmueller, M. Kundi, M. Haider, Clastogenic effects of radiofrequency radiations on chromosomes of *Tradescantia*, Mutat. Res. 324 (1–2) (1994) 65–68.

[58] H. Lai, M.A. Carino, N.P. Singh, Naltrexone blocks RFR-induced DNA double strand breaks in rat brain cells, Wireless Netw. 3 (1997) 471–476.

[59] H. Lai, N.P. Singh, Acute low-intensity microwave exposure increases DNA singlestrand breaks in rat brain cells, Bioelectromagnetics 16 (3) (1995) 207–210.

[60] H. Lai, N.P. Singh, Interaction of microwaves and a temporally incoherent magnetic field on single and double DNA strand breaks in rat brain cells, Electromagn. Biol. Med. 24 (1) (2005) 23–29.

[61] H. Lai, N.P. Singh, Single- and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation, Int. J. Radiat. Biol. 69 (4) (1996) 513–521.

[62] S. Lixia, K. Yao, W. Kajun, L. Dqiang, H. Huajun, G. Xiangwei, W. Baohong, Z. Wie, L. Jianling, W. Wie, Effects of 1.8 GHz radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells, Mutat. Res. 602 (2006) 135–142.

[63] A. Maes, M. Collier, D. Slaets, L. Verschaeve, Cytogenic effects of microwaves from mobile communication frequencies (954 MHz), Electro Magnetobiol. 14 (2) (1995) 91–98.

[64] A. Maes, L. Verschaeve, A. Arroyo, C. De Wagter, L. Vercruyssen, In vitro cytogenetic effects of 2450 MHz waves on human peripheral blood lymphocytes, Bioelectromagnetics 14 (6) (1993) 495–501.

[65] E. Markova, L. Hillert, L. Malmgren, B.R. Persson, I.Y. Belyaev, Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons, Environ. Health Perspect. 113 (9) (2005) 1172–1177.

[66] M. Mashevich, D. Folkman, A. Kesar, A. Barbul, R. Korenstein, E. Jerby, L. Avivi, Exposure of human peripheral blood lymphocytes to electromagnetic fields associated with cellular phones leads to chromosomal instability, Bioelectromagnetics 24 (2) (2003) 82–90.

[67] T. Nikolova, J. Czyz, A. Rolletschek, P. Blyszczuk, J. Fuchs, G. Jovtchev, J. Schuderer, N. Kuster, A.M. Wobus, Electromagnetic fields affect transcript levels apoptosis-related genes in embryonic stem cell-derived neural progenitor cells, FASEB J. 19 (2005) 1686–1688.

[68] R. Paulraj, J. Behari, Single strand DNA breaks in rat brain cells exposed to microwave radiation, Mutat. Res. 596 (1–2) (2006) 76–80.

[69] J.L. Phillips, O. Ivaschuk, T. Ishida-Jones, R.A. Jones, M. Campbell-Beachler, W. Haggren, DNA damage in Molt-4 T-lymphoblastoid cells exposed to cellular 27 telephone radiofrequency fields in vitro, Bioelectrochem. Bioenerg. 45 (1) (1998) 103–110.

[70] R. Sarimov, L.O.G. Malmgren, E. Markova, B.R.R. Persson, I.Y. Belyaev, Nonthermal GSM microwaves affect chromatin conformation in human lymphocytes similar to heat shock, IEEE Trans. Plasma Sci. 32 (2004) 1600–1608.

[71] S. Sarkar, S. Ali, J. Behari, Effect of low power microwave on the mouse genome: a direct DNA analysis, Mutat. Res. 320 (1–2) (1994) 141–147.

[72] R.R. Tice, G.G. Hook, M. Donner, D.I. McRee, A.W. Guy, Genotoxicity of radiofrequency signals. I. Investigation of DNA damage and micronuclei induction in cultured human blood cells, Bioelectromagnetics 23 (2) (2002) 113–126.

[73] I. Trosic, I. Busljeta, V. Kasuba, R. Rozgaj, Micronucleus induction after whole-body microwave irradiation of rats, Mutat. Res. 521 (1–2) (2002) 73–79.

[74] I. Trosic, I. Busljeta, B. Modlic, Investigation of the genotoxic effect of microwave irradiation in rat bone marrow cells: in vivo exposure, Mutagenesis 19 (5) (2004) 361–364.

[75] I. Trosic, I. Busljeta, Erythropoietic dynamic equilibrium in rats maintained after microwave irradiation, Exp. Toxicol. Pathol. 57 (3) (2006) 247–251.

[76] Vijayalaxmi, M.R. Frei, S.J. Dusch, V. Guel, M.L. Meltz, J.R. Jauchem, Frequency of micronuclei in the peripheral blood and bone marrow of cancer-prone mice chronically exposed to 2450 MHz radiofrequency radiation, Radiat. Res. 147 (4) (1997) 495–500.

[77] D.Y. Zhang, Z.P. Xu, H. Chiang, D.Q. Lu, Q.L. Zeng, Effects of GSM 1800 MHz radiofrequency electromagnetic fields on DNA damage in Chinese hamster lung cells., Zhonghua Yu Fang Yi Xue Za Zhi 40 (3) (2006) 149–152 (in Chinese).

[78] L. Zotti-Martelli, M. Peccatori, V. Maggini, M. Ballardin, R. Barale, Individual responsiveness to induction of micronuclei in human lymphocytes after exposure in vitro to 1800-MHz microwave radiation, Mutat. Res. 582 (1–2) (2005) 42–52.

[79] L. Zotti-Martelli, M. Peccatori, R. Scarpato, L. Migliore, Induction of micronuclei in human lymphocytes exposed in vitro to microwave radiation, Mutat. Res. 472 (1–2) (2000) 51–58.

[80] A. Antonopoulos, H. Eisenbrandt, G. Obe, Effects of high-frequency electromagnetic fields on human lymphocytes in vitro, Mutat. Res. 395 (2–3) (1997) 209–214.

[81] I.Y. Belyaev, C.B. Koch, O. Terenius, K. Roxstrom-Lindquist, L.O.G. Malmgren, W.H. Sommer, L.G. Salford, B.R.R. Persson, Exposure of rat brain to 915 MHz GSM microwaves induces changes in gene expression but not double stranded DNA breaks or effects on chromatin conformation, Bioelectromagnetics 27 (4) (2006) 295–306.

[82] K.S. Bisht, E.G. Moros, W.L. Straube, J.D. Baty, J.L. Roti Roti, The effect of 835.62 MHz FDMA or 847.74 MHz CDMA modulated radiofrequency rad on the induction of micronuclei in C3H 10T1/2 cells, Radiat. Res. 157 (5) (2002) 506–515.

[83] S.K. Chang, J.S. Choi, H.W. Gil, J.O. Yang, E.Y. Lee, Y.S. Jeon, Z.W. Lee, M. Lee, M.Y. Hong, T. Ho Son, S.Y. Hong, Genotoxicity evaluation of electromagnetic fields generated by 835-MHz mobile phone frequency band, Eur. J. Cancer Prev. 14 (2) (2005) 175–179.

[84] V. Ciaravino, M.L. Meltz, D.N. Erwin, Absence of a synergistic effect between moderate-power radio-frequency electromagnetic radiation and adriamycin on cellcycle progression and sister-chromatid exchange, Bioelectromagnetics 12 (5) (1991) 289–298.

[85] O.M. Garson, T.L. McRobert, L.J. Campbell, B.A. Hocking, I. Gordon, A chromosomal study of workers with long-term exposure to radio-frequency radiation, Med. J. Aust. 155 (5) (1991) 289–292.

[86] B.D. Gorlitz, M. Muller, S. Ebert, H. Hecker, N. Kuster, C. Dasenbrock, Effects of 1-week and 6-week exposure to GSM/DCS radiofrequency radiation on micronucleus formation in B6C3F1 mice, Radiat. Res. 164 (4 Pt 1) (2005) 431–439.

[87] P. Gos, B. Eicher, J. Kohli, W.D. Heyer, No mutagenic or recombinogenic effects of mobile phone fields at 900 MHz detected in the yeast *Saccharomyces cerevisiae*, Bioelectromagnetics 21 (7) (2000) 515–523.

[88] G.J. Hook, P. Zhang, I. Lagroye, L. Li, R. Higashikubo, E.G. Moros, W.L. Straube, W.F. Pickard, J.D. Baty, J.L. Roti Roti, Measurement of DNA damage and apoptosis in molt-4 cells after in vitro exposure to radiofrequency radiation, Radiat. Res. 161 (2) (2004) 193–200.

[89] J. Juutilainen, P. Heikkinen, H. Soikkeli, J. Maki-Paakanen, Micronucleus frequency in erythrocytes of mice after long-term exposure to radiofrequency radiation, Int. J. Radiat. Biol. 83 (2007) 213–220.

[90] J.J. Kerbacher, M.L. Meltz, D.N. Erwin, Influence of radiofrequency radiation on chromosome aberrations in CHO cells and its interaction with DNA-damaging agents, Radiat. Res. 123 (3) (1990) 311–319.

[91] Y. Komatsubara, H. Hirose, T. Sakurai, S. Koyama, Y. Suzuki, M. Taki, J. Miyakoshi, Effect of high-frequency electromagnetic fields with a wide range of SARs on chromosomal aberrations in murine m5S cells, Mutat. Res. 587 (1–2) (2005) 114–119.

[92] S. Koyama, Y. Isozumi, Y. Suzuki, M. Taki, J. Miyakoshi, Effects of 2.45-GHz electromagnetic fields with a wide range of SARs on micronucleus formation in CHO-K1 cells, Sci. World J. 4 (Suppl. 2) (2004) 29–40.

[93] I. Lagroye, R. Anane, B.A. Wettring, E.G. Moros, W.L. Straube, M. Laregina, M. Niehoff, W.F. Pickard, J. Baty, J.L. Roti, Measurement of DNA damage after acute exposure to pulsed-wave 2450 MHz microwaves in rat brain cells by two alkaline comet assay methods, Int. J. Radiat. Biol. 80 (1) (2004) 11–20.

[94] I. Lagroye, G.J. Hook, B.A. Wettring, J.D. Baty, E.G. Moros, W.L. Straube, J.L. Roti Roti, Measurements of alkali-labile DNA damage and protein–DNA crosslinks after 2450 MHz microwave and low-dose gamma irradiation in vitro, Radiat. Res. 161 (2) (2004) 201–214.

[95] L. Li, K.S. Bisht, I. LaGroye, P. Zhang, W.L. Straube, E.G. Moros, J.L. Roti Roti, Measurement of DNA damage in mammalian cells exposed in vitro to radiofrequency fields at SARs of 3–5 W/kg, Radiat. Res. 156 (3) (2001) 328–332.

[96] A. Maes, M. Collier, L. Verschaeve, Cytogenetic effects of 900 MHz (GSM) microwaves on human lymphocytes, Bioelectromagnetics 22 (2) (2001) 91–96.

[97] A. Maes, M. Collier, L. Verschaeve, Cytogenetic investigations on microwaves emitted by a 455.7 MHz car phone, Folia Biol. (Praha) 46 (5) (2000) 175–180.

[98] A. Maes, U. Van Gorp, L. Verschaeve, Cytogenetic investigation of subjects professionally exposed to radiofrequency radiation, Mutagenesis 21 (2) (2006) 139–142.

[99] R.S. Malyapa, E.W. Ahern, C. Bi, W.L. Straube, M. LaRegina, W.F. Pickard, J.L. Roti Roti, DNA damage in rat brain cells after in vivo exposure to 2450 MHz electromagnetic radiation and various methods of euthanasia, Radiat. Res. 149 (6) (1998) 637–645.

[100] R.S. Malyapa, E.W. Ahern, W.L. Straube, E.G. Moros, W.F. Pickard, J.L. Roti Roti, Measurement of DNA damage after exposure to 2450 MHz electromagnetic radiation, Radiat. Res. 148 (6) (1997) 608–617.

[101] R.S. Malyapa, E.W. Ahern, W.L. Straube, E.G. Moros, W.F. Pickard, J.L. Roti Roti, Measurement of DNA damage after exposure to electromagnetic radiation in the cellular phone communication frequency band (835.62 and 847.74 MHz), Radiat. Res. 148 (6) (1997) 618–627.

[102] J.P. McNamee, P.V. Bellier, G.B. Gajda, et al., No evidence for genotoxic effects from 24 h exposure of human leukocytes to 1.9 GHz radiofrequency fields, Radiat. Res. 159 (2003) 693–697.

[103] J.P. McNamee, P.V. Bellier, G.B. Gajda, B.F. Lavallee, E.P. Lemay, L. Marro, A. Thansandote, DNA damage in human leukocytes after acute in vitro exposure to a 1.9 GHz pulse-modulated radiofrequency field, Radiat. Res. 158 (4) (2002) 534–537.

[104] J.P. McNamee, P.V. Bellier, G.B. Gajda, S.M. Miller, E.P. Lemay, B.F. Lavallee, L. Marro, A. Thansandote, DNA damage and micronucleus induction in human leukocytes 24 after acute in vitro exposure to a 1.9 GHz continuous-wave radiofrequency field, Radiat. Res. 158 (4) (2002) 523–533.

[105] M.L. Meltz, P. Eagan, D.N. Erwin, Proflavin and microwave radiation: absence of a mutagenic interaction, Bioelectromagnetics 11 (2) (1990) 149–157.

[106] T. Ono, Y. Saito, J. Komura, H. Ikehata, Y. Tarusawa, T. Nojima, K. Goukon, Y. Ohba, J. Wang, O. Fujiwara, R. Sato, Absence of mutagenic effects of 2.45 GHz radiofrequency exposure in spleen, liver, brain, and testis of lacZ-transgenic mouse exposed in utero, Tohoku J. Exp. Med. 202 (2) (2004) 93–103.

[107] J.L. Roti Roti, R.S. Malyapa, K.S. Bisht, E.W. Ahern, E.G. Moros, W.F. Pickard, W.L. Straube, Neoplastic transformation in C3H 10T(1/2) cells after exposure to 835.62 MHz FDMA and 847.74 MHz CDMA radiations, Radiat. Res. 155 (1) (2001) 239–247.

[108] N. Sakuma, Y. Komatsubara, H. Takeda, H. Hirose, M. Sekijima, T. Nojima, J. Miyakoshi, DNA strand breaks are not induced in human cells exposed to 2.1425 GHz band CW and W-CDMA modulated radiofrequency fields allocated to mobile radio base stations, Bioelectromagnetics 27 (1) (2006) 51–57.

[109] M.R. Scarfi, A.M. Fresegna, P. Villani, R. Pinto, C. Marino, M. Sarti, P. Altavista, A. Sannino, G.A. Lovisolo, Exposure to radiofrequency radiation (900 MHz, GSM signal) does not affect micronucleus frequency and cell proliferation in human peripheral blood lymphocytes: an interlaboratory study, Radiat. Res. 165 (6) (2006) 655–663.

[110] L. Stronati, A. Testa, J. Moquet, A. Edwards, E. Cordelli, P. Villani, C. Marino, A.M. Fresegna, M. Appolloni, D. Lloyd, 935 MHz cellular phone radiation. An in vitro study of genotoxicity in human lymphocytes, Int. J. Radiat. Biol. 82 (5) (2006) 339–346.

[111] S. Takahashi, S. Inaguma, Y.-M. Cho, K. Imaida, J. Wang, O. Fujiwara, T. Shirai, Lack of mutation induction with exposure to 1.5 GHz electromagnetic near fields used for cellular phones in brains of Big Blue mice, Cancer Res. 62 (7) (2002) 1956–1960.

[112] L. Verschaeve, P. Heikkinen, G. Verheyen, U. Van Gorp, F. Boonen, F. Vander Plaetse, A. Maes, T. Kumlin, J. Maki-Paakkanen, L. Puranen, J. Juutilainen, Investigation of co-genotoxic effects of radiofrequency electromagnetic fields in vivo, Radiat. Res. 165 (5) (2006) 598–607.

[113] Vijayalaxmi, B.Z. Leal, M.L. Meltz, W.F. Pickard, K.S. Bisht, J.L. Roti Roti, W.L. Straube, E.G. Moros, Cytogenetic studies in human blood lymphocytes exposed in vitro to radiofrequency radiation at a cellular telephone frequency (835.62 MHz, FDMA), Radiat. Res. 155 (1) (2001) 113–121.

[114] Vijayalaxmi, K.S. Bisht, W.F. Pickard, M.L. Meltz, J.L. Roti Roti, E.G. Moros, Chromosome damage and micronucleus formation in human blood lymphocytes exposed in vitro to radiofrequency radiation at a cellular telephone frequency (847.74 MHz, CDMA), Radiat. Res. 156 (4) (2001) 430–432.

[115] Vijayalaxmi, B.Z. Leal, M. Szilagyi, T.J. Prihoda, M.L. Meltz, Primary DNA damage in human blood lymphocytes exposed in vitro to 2450 MHz radiofrequency radiation, Radiat. Res. 153 (4) (2000) 479–486.

[116] Vijayalaxmi, N. Mohan, M.L. Meltz, M.A. Wittler, Proliferation and cytogenetic studies in human blood lymphocytes exposed in vitro to 2450 MHz radiofrequency radiation, Int. J. Radiat. Biol. 72 (6) (1997) 751–757.

[117] Vijayalaxmi, W.F. Pickard, K.S. Bisht, T.J. Prihoda, M.L. Meltz, M.C. LaRegina, J.L. Roti Roti, W.L. Straube, E.G. Moros, Micronuclei in the peripheral blood and bone marrow cells of rats exposed to 2450 MHz radiofrequency radiation, Int. J. Radiat. Biol. 77 (11) (2001) 1109–1115.

[118] Vijayalaxmi, L.B. Sasser, J.E. Morris, B.W. Wilson, L.E. Anderson, Genotoxic potential of 1.6 GHz wireless communication signal: in vivo two-year bioassay, Radiat. Res. 159 (4) (2003) 558–564.

[119] Vijayalaxmi, R.L. Seaman, M.L. Belt, J.M. Doyle, S.P. Mathur, T.J. Prihoda, Frequency of micronuclei in the blood and bone marrow cells of mice exposed to ultrawideband electromagnetic radiation, Int. J. Radiat. Biol. 75 (1) (1999) 115–120.

[120] O. Zeni, M. Romano, A. Perrotta, M.B. Lioi, R. Barbieri, G. d'Ambrosio, R. Massa, M.R. Scarfi, Evaluation of genotoxic effects in human peripheral blood leukocytes following an acute in vitro exposure to 900 MHz radiofrequency fields, Bioelectromagnetics 26 (4) (2005) 258–265.

[121] O. Zeni, A.S. Schiavoni, A. Sannino, A. Antolini, D. Forigo, F. Bersani, M.R. Scarfi, Lack of genotoxic effects (micronucleus induction) in human lymphocytes exposed in vitro to 900 MHz electromagnetic fields, Radiat. Res. 160 (2) (2003) 152–158.

[122] W. Baohong, H. Jiliang, J. Lifen, L. Deqiang, Z. Wei, L. Jianlin, D. Hongping, Studying the synergistic damage effects induced by 1.8 GHz radiofrequency field radiation (RFR) with four chemical mutagens on human lymphocyte DNA using comet assay in vitro, Mutat. Res. 578 (1–2) (2005) 149–157.

[123] W. Baohong, J. Lifen, L. Lanjuan, L. Jianlin, L. Deqiang, Z. Wie, H. Jillang, Evaluating the combinative effects on human lymphocyte DNA damage induced by ultraviolet ray C plus 1.8 GHz microwaves using comet assay in vitro, Toxicology 232 (2007) 311–316.

[124] J.Y. Kim, S.Y. Hong, Y.M. Lee, W.S. Koh, J.R. Hong, T. Son, S.K. Chang, M. Lee, In vitro assessment of clastogenicity of mobile-phone radiation (835 MHz) using the alasline comet assay and chromosomal aberration test, Environ. Toxicol. 23 (2008) 319–327.

[125] A. Maes, M. Collier, D. Slaets, L. Verschaeve, 954 MHz microwaves enhance the mutagenic properties of mitomycin C, Environ. Mol. Mutagen. 28 (1) (1996) 26–30.

[126] A. Maes, M. Collier, U. Van Gorp, S. Vandoninck, L. Verschaeve, Cytogenetic effects of 935.2-MHz (GSM) microwaves alone and in combination with mitomycin C, Mutat. Res. 393 (1–2) (1997) 151–156.

[127] B.H. Wang, D.Q. Lu, L.F. Jin, S.J. Chen, J.L. Lou, J.L. He, Influence of 1.8 GHz microwave on DNA damage induced by ultraviolet C ray, Zhonghua Lao Dong Wie Sheng Zhi Ye Bing Za Zhi 25 (2007) 470–472 (Chinese language).

[128] B.H. Wang, D.Q. Lu, L.F. Jin, W. Zheng, J.L. Lou, H.P. Deng, Q.Y. Li, J.L. He, Influence of 1.8 GHz microwave on DNA damage induced by 4 chemical mutagens, Zhonghua Lao Dong Wie Sheng Zhi Ye Bing Za Zhi 23 (2005) 163–166.

[129] M.B. Zhang, J.L. He, L.F. Jin, D.Q. Lu, Study of low-intensity 2450-MHz microwave exposure enhancing the genotoxic effects of mitomycin C using micronucleus test and comet assay in vitro, Biomed. Environ. Sci. 15 (4) (2002) 283–290.

ELSEVIER

Pathophysiology 16 (2009) 103–112

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Increased blood–brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone

Henrietta Nittby[a,*], Arne Brun[b], Jacob Eberhardt[c], Lars Malmgren[d], Bertil R.R. Persson[c], Leif G. Salford[a]

[a] *Department of Neurosurgery, Lund University, The Rausing Laboratory and Lund University Hospital, S-22185, Lund, Sweden*
[b] *Department of Neuropathology, Lund University, The Rausing Laboratory and Lund University Hospital, S-22185, Lund, Sweden*
[c] *Department of Medical Radiation Physics, Lund University, The Rausing Laboratory and Lund University Hospital, S-22185, Lund, Sweden*
[d] *The MAX Laboratory, Lund University, The Rausing Laboratory and Lund University Hospital, S-22185, Lund, Sweden*

Received 17 December 2008; accepted 30 January 2009

Abstract

Microwaves were for the first time produced by humans in 1886 when radio waves were broadcasted and received. Until then microwaves had only existed as a part of the cosmic background radiation since the birth of universe. By the following utilization of microwaves in telegraph communication, radars, television and above all, in the modern mobile phone technology, mankind is today exposed to microwaves at a level up to 10^{20} times the original background radiation since the birth of universe.

Our group has earlier shown that the electromagnetic radiation emitted by mobile phones alters the permeability of the blood–brain barrier (BBB), resulting in albumin extravasation immediately and 14 days after 2 h of exposure.

In the background section of this report, we present a thorough review of the literature on the demonstrated effects (or lack of effects) of microwave exposure upon the BBB.

Furthermore, we have continued our own studies by investigating the effects of GSM mobile phone radiation upon the blood–brain barrier permeability of rats 7 days after one occasion of 2 h of exposure. Forty-eight rats were exposed in TEM-cells for 2 h at non-thermal specific absorption rates (SARs) of 0 mW/kg, 0.12 mW/kg, 1.2 mW/kg, 12 mW/kg and 120 mW/kg. Albumin extravasation over the BBB, neuronal albumin uptake and neuronal damage were assessed.

Albumin extravasation was enhanced in the mobile phone exposed rats as compared to sham controls after this 7-day recovery period (Fisher's exact probability test, $p = 0.04$ and Kruskal–Wallis, $p = 0.012$), at the SAR-value of 12 mW/kg (Mann–Whitney, $p = 0.007$) and with a trend of increased albumin extravasation also at the SAR-values of 0.12 mW/kg and 120 mW/kg. There was a low, but significant correlation between the exposure level (SAR-value) and occurrence of focal albumin extravasation ($r_s = 0.33$; $p = 0.04$).

The present findings are in agreement with our earlier studies where we have seen increased BBB permeability immediately and 14 days after exposure. We here discuss the present findings as well as the previous results of altered BBB permeability from our and other laboratories.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Albumin; Blood–brain barrier; Mobile phone; Rat

1. Introduction: radiofrequency radiation and the blood–brain barrier

Today about half of the world's population owns the microwave-producing mobile phones. An even larger number is exposed to the radiation emitted from these devices through "passive mobile phoning" [1]. Life-long exposure to the microwaves (MWs) from mobile phones, with start already at a young age, is becoming increasingly common

Abbreviations: BBB, blood–brain barrier; CNS, central nervous system; CW, continuous wave; EMF, electromagnetic field; GSM, global system for mobile communication; ICNIRP, International Commission of Non-ionizing Radiation Protection; MRI, magnetic resonance imaging; RF, radio frequency; SAR, specific absorption rate; TEM-cell, transverse electromagnetic transmission line chamber.

* Corresponding author. Tel.: +46 46 173922; fax: +46 46 188150.
E-mail address: henrietta.nittby@med.lu.se (H. Nittby).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.001

among the new generations of mobile phone users. The question is: to what extent are living organisms affected by these radio frequency (RF) fields?

The mobile phones are held in close proximity to the head, or within a metre of the head when hands-free sets are used. The emitted microwaves have been shown to have many effects upon the mammalian brain; e.g. alterations of cognitive functions [2,3], changes of neurotransmitter levels such as decrease of cholinergic activity [4], gene expression alterations in cerebellum [5], cortex and hippocampus [6], and impact upon the brain EEG activity [7]. Also, the human brain EEG beta rhythms energies were increased by exposure to 450 MHz MWs modulated at different low frequencies [8]. Recent epidemiological studies also indicate that long-term exposure increases the risk of not only for benign vestibular schwannoma (previously named acoustic neurinoma) [9], but also malignant glioblastoma multiforme [10] for mobile phone use longer than 10 years and with cumulative exposure from mobile phones exceeding 2000 h.

It has been shown that electromagnetic fields (EMFs) increase the permeability of the blood–brain barrier (BBB) (for reference see [11]). The BBB is a hydrophobic barrier, formed by vascular endothelial cells of the capillaries in the brain, with tight junctions between these endothelial cells. It protects the mammalian brain from potentially harmful compounds in the blood. Also, perivascular structures such as astrocytes and pericytes as well as a bi-layered basal membrane help maintaining the BBB.

The current recommendations for limits of exposure to the general public for EMF radiation [12] are set in order to avoid thermal effects upon the brain parenchyma.

In our previous studies we have seen that non-thermal RF fields cause significantly increased leakage of the rats' own albumin through the BBB of exposed rats sacrificed immediately after the exposure, as compared to sham exposed control animals [11,13–18]. Two hours of exposure to the radiation from a global system for mobile communications (GSM) phone at 915 MHz, at non-thermal specific absorption rates (SAR) values of 0.12 mW/kg, 12 mW/kg and 120 mW/kg, gives rise to focal albumin extravasation and albumin uptake into neurons also 14 days after exposure, but not after 28 days [19]. Significant neuronal damage is present 28 days [19] and 50 days after exposure [20], but not after 14 days [19]. Also, in experiments from other laboratories, BBB permeability is increased in connection to mobile phone exposure [21–23] and other kinds of EMF such as magnetic resonance imaging (MRI) exposure [24–26]. In other studies, no such BBB alterations have been demonstrated in connection to mobile phone exposure [27–29] or other kinds of EMF exposure [30,31].

1.1. The blood–brain barrier

An intact BBB is necessary for the protection of the mammalian brain from potentially harmful substances circulating in the blood. In the normal brain, the passage of compounds over the BBB is highly restricted and homeostasis within the sensitive environment of the brain parenchyma can be maintained.

The BBB is formed by the vascular endothelial cells of the capillaries of the brain and the glial cells wrapped around them. The tight junctions, that seal the endothelial cells together, limit paracellular leakage of molecules. A bi-layered basal membrane supports the ablumenal side of the endothelial cells. The glial astrocytes, surrounding the surface of the basal membrane cells, are important for the maintenance, functional regulation and repair of the BBB. The protrusions of the astrocytes, called end feet, cover the basal membrane on the outer endothelial surface and thus form a second barrier to hydrophilic molecules and connect the endothelium to the neurons. Twenty-five per cent of the ablumenal membrane of the capillary surface is covered by pericytes [32], which are a type of macrophages. Seemingly, they are in the position to significantly contribute to the central nervous system (CNS) immune mechanisms [33].

The physiological properties of the CNS microvasculature are different from those of peripheral organs. The numbers of pinocytotic vesicles for nutrient transport through the endothelial cytoplasm are low and there are no fenestrations. Also, there is a fivefold higher number of mitochondria in the BBB endothelial cells as compared to muscular endothelial cells [34].

In a functioning BBB, the membrane properties control the bidirectional exchange between the general circulation and the CNS. Water, most lipid-soluble molecules, oxygen and carbon dioxide can diffuse from the blood to the nerve cells. The barrier is slightly permeable to ions such as sodium, potassium and chloride, but large molecules, such as proteins and most water-soluble chemicals only pass poorly. However, when this barrier is damaged, in conditions such as tumours, infarcts or infections, also the normally excluded molecules can pass through, possibly bringing toxic molecules out into the brain tissue. The selective permeability is disrupted temporally in cases of epileptic seizures [35,36] and severe hypertension [37]. The result of this can be cerebral oedema, increased intracranial pressure and irreversible brain damage. Also, toxic substances from the blood circulation now reach out to the neurons. Even transient openings of the BBB can lead to permanent tissue damage [37].

1.2. The earliest studies on the effects of microwave exposure

The first studies on the MW effects upon the BBB were reported in the 1970s, when the radiation from radars and MW ovens were considered to be possible health threats. Increased leakage of fluorescein after 30 min of pulsed and CW exposure [38] and passage of ^{14}C-mannitol, inulin and dextran at very low energy levels [39] were reported. The permeation of mannitol was found to be a definite function of exposure parameters such as power density, pulse width, and the number of pulses per second. Also, the BBB permeability depended on the time between the EMF exposure and the

sacrifice of the animals, with more pronounced effects seen in the animals sacrificed earlier after the EMF exposure. In attempts to replicate the findings of Oscar and Hawkins [39], however, these results were not found [40,41]. Similar lack of MW induced BBB effects, was reported by Ward et al. [42] after exposure of rats to CWs at 2450 MHz; Ward and Ali [43] after exposure at 1.7 GHz; and Gruenau et al. [44] after exposure to pulsed or CW waves at 1.8 GHz (including totally 31 rats). On the other hand, Albert and Kerns [45] observed EMF-induced BBB permeability after exposure at 2450 MHz CWs, with an increase in the number of pinocytotic vesicles among the irradiated animals, but after a recovery time of 1–2 h, the permeation was hardly detectable anymore. For details concerning the EMF exposure parameters in these studies, see [11].

1.3. MRI exposure

MRI entails a concurrent exposure to a high-intensity static field, a RF field and a time-varying magnetic field. In connection to the introduction of the MRI technique, the effects of exposure to these kinds of fields upon the BBB permeability were investigated.

As mentioned above, Shivers et al. [24] observed that the EMF exposure of the type emitted during a MRI procedure resulted in a temporarily increased BBB permeability in the brains of rats. Through transendothelial channels, a vesicle-mediated transport of horseradish peroxidase (HRP) took place. Replications of the initial findings by Shivers et al. [24] were made by Garber et al. [46], whereas Adzamli et al. [30] and Preston et al. [31] could not repeat the findings.

After some years, quantitative support of the findings by Shivers et al. [24] was presented by the same group [25,26]. In rats exposed to the MRI, the BBB permeability to DTPA (diethylenetriameninepentaacetic acid) increased. A suggested mechanism explaining the increased permeability was a stimulation of endocytosis, made possible through the time-varying magnetic fields.

Also our studies supported the findings of the Shiver–Prato group; seeing that BBB permeability to albumin was increased after exposure to MRI radiation [13]. The most significant effect was observed after exposure to the RF part of the MRI.

1.4. Studies on mobile phone exposure

The mobile phone induced effects upon the BBB permeability is a topic of importance for the whole society today. We have previously found an increased BBB permeability immediately after 2 h of mobile phone exposure [14], and also after 14 days [19] and 50 days [20].

Repetitions of our findings of increased BBB permeability after mobile phone exposure have been made [47,21,22]. Four hours of GSM-900 MHz exposure at brain power densities ranging from 0.3 to 7.5 W/kg resulted in significantly increased albumin extravasation both at the SAR-value of 7.5 W/kg, which is a thermal effect, but also at 0.3 W/kg and 1.3 W/kg [47] (statistical evaluations discussed by Salford et al. [1]). Albumin extravasation was also seen in rats exposed for 2 h to GSM-900 MHz at non-thermal SAR-values of 0.12, 0.5 and 2 W/kg using fluorescein-labelled proteins [21,22]. At SAR of 2 W/kg a marked BBB permeabilization was observed, but also at the lower SAR-value of 0.5 W/kg, permeabilization was present around intracranial blood vessels. However, the extravasation at 0.5 W/kg was seen at a lesser extent as compared to that seen at 2 W/kg. Subgroups of the rats included in these studies were sympathectomised, which means that they were in a chronic inflammation-prone state with increased BBB opening due to changes in the structures of the blood vessels. Interestingly, the sympathectomised rats exposed to GSM radiation had a remarkable increase of the BBB leakage as compared to their sympathectomised sham controls. From these findings it seems likely that an already disrupted BBB is more sensitive to the RF fields than an intact BBB.

In another study, the uptake of rhodamine–ferritin complex through the BBB was investigated [23]. In this study, increased BBB permeability was clearly seen at exposure levels of 2 W/kg and durations of 30–120 min. When the rats were pre-treated with colchicine, the EMF-induced rhodamine–ferritin uptake was however blocked. Colchicine is well-known for its inhibition of microtubular function. It was concluded that the microtubules seemed to play an important role for the BBB opening.

Lack of EMF-induced BBB alterations has also been reported [27–29,48]. In a small study including only 12 EMF exposed animals, no albumin extravasation was seen, neither after 2 nor 4 weeks of 1 h of daily exposure (average whole-body exposure at 0.25 W/kg) [27]. In a study including 40 animals, Kuribayashi et al. [28] concluded no BBB alterations was seen after 90 min of daily EMF exposure for 1–2 weeks at SAR-values of 2 or 6 W/kg. Finnie et al. [29] exposed mice for 1 h daily. However, only the SAR-value of 4 W/kg, which is above the ICNIRP limit [12], was included. In a further study by Finnie et al. [48] 207 mice were exposed for 104 weeks at SAR-values of 0.25–4 W/kg, however without any observable effects upon the BBB permeability. The same group also reported that the immature BBB was insensitive to mobile phone exposure, seen after GSM-900 radiation exposure of pregnant mice from day 1 to day 19 of gestation (SAR of 4 W/kg, exposure for 60 min daily). No increased albumin extravasation was seen in the new-born mice immediately after parturition [49] and the same lack of GSM-900 radiation effects upon the BBB permeability was reported for young rats by Kumlin et al. [50], however, in this case only 12 out of totally 48 exposed rats were analyzed histopathologically. The remaining rats were subject to memory tests, where an improved learning and memory was seen in the EMF exposed rats as compared to the sham controls. Notably, in all these studies, the SAR-values for exposure are relatively high; never including the low SAR-values below 200 mW/kg.

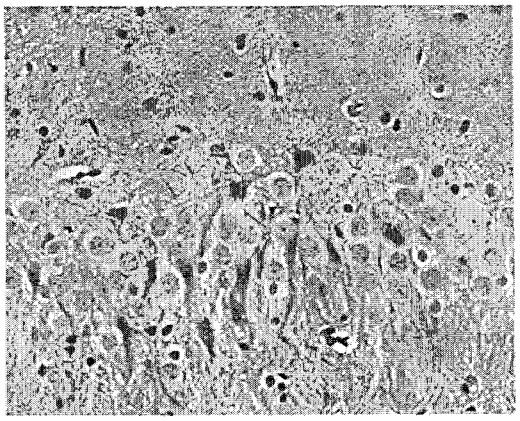


Fig. 1. Albumin neuronal uptake and early neuronopathy in the hippocampal pyramidal cell row among normal neurons. Albumin: cresyl violet, ×20.

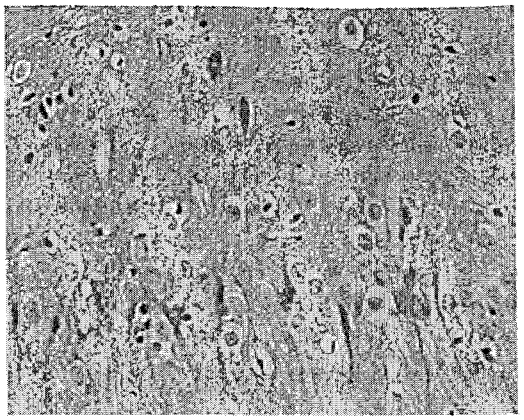


Fig. 2. Shrunken homogenized dark neurons with brownish discoloration due to uptake of albumin, interspersed among normal neurons in the hippocampal pyramidal cell row. Albumin: cresyl violet, ×20. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

In more recent years, *in vitro* models have been increasingly applied to investigate the BBB; in one of these, it was shown that EMFs at 1.8 GHz increase the permeability to sucrose [51]. After modifications of the BBB model to one with higher tightness, however, the same group could not replicate their initial findings [52]. With application of the EMF of the kind emitted from 3G mobile phones, the same group further concluded that their *in vitro* BBB model also did not alter its tightness or transport behaviour in connection to this type of exposure [53].

1.5. Neuronal damage in connection to mobile phone exposure

In our previous studies of animals surviving a longer period after the exposure, we have evaluated the occurrence of neuronal damage extensively [19,20]. This neuronal damage is seen as condensed dark neurons. Dark neurons have been proposed to have three main characteristics [54]: (i) irregular cellular outlines, (ii) increased chromatin density in the nucleus and cytoplasm and (iii) intensely and homogenously stained nucleus. Twenty-eight days after 2 h of mobile phone exposure, the neuronal damage was significantly increased in the exposed rats as compared to the sham exposed controls [19]. Also 50 days after the same kind of mobile phone exposure, there was an increased occurrence of neuronal damage [20].

In our studies, normal neurons have been shown to have increased uptake of albumin [19] (Fig. 1). Also, in dark neurons this neuronal albumin uptake can be seen (Fig. 2). In our previous studies, damaged neurons were seen in all locations, intermingled with normal neurons especially in the cortex, hippocampus and basal ganglia. The damaged neurons were often shrunken and dark staining, homogenized with loss of discernable internal cell structures (Fig. 3). Some damaged neurons showed microvacuoles in the cytoplasm (Fig. 4). These vacuoles are a sign of severe neuronopathy, indicating an active pathological process. There was no evidence of haemorrhages or glial reaction.

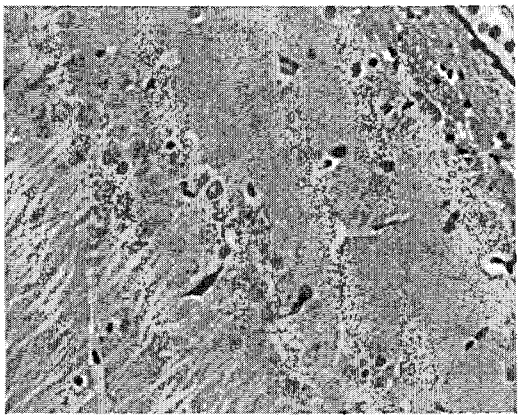


Fig. 3. Two dark neurons in the hippocampal pyramidal cell row. Albumin: cresyl violet, ×20.

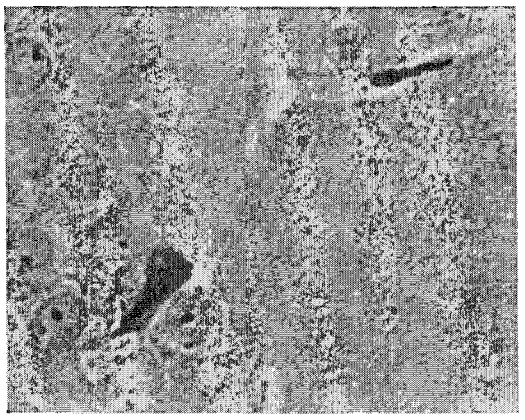


Fig. 4. Dark neuron in the hippocampal pyramidal cell row, with homogenized nucleus and cytoplasm with a vacuole. Higher magnification of part of the figure. Albumin: cresyl violet, ×40.

Dark neurons are reported in clinical and experimental neuropathology from living tissues, but not in autopsy material unless the post-mortem period is short. This could indicate that the formation of dark neurons is an active process that requires living neurons and that these cells must be reasonably intact [55]. This could be in accordance with our findings from the 50-days survival animals, where apoptosis could not be detected in any of the RF EMF exposed brains with application of Caspase-3 [56].

Dark neurons occur not only after GSM exposure [19,20] but also in connection to experimental ischemia [57], hypoglycemia [58] and epilepsy [59]. Possibly, dark neurons could be artefacts, having a pressure-derived mechanical origin, as has been shown for cortical biopsies (this is less likely considering the atraumatic method of dissection used here including fixation before handling and in view of the deep location of the dark neurons). However, dark neurons also appear as a result of other, and not fully clarified, mechanisms, as seen in the case of GSM exposure, ischemia, hypoglycemia and epilepsy. A pharmacologic origin, such as depolarization related to tissue glutamate release in injury, could explain the pathogenetic mechanism for dark neurons in these cases, rather than the pressure-derived mechanical origin. Indeed, the formation of dark neurons can be prevented using pharmacologic forms of glutamate antagonism [55]. In the case of our studies, our technique for the resection of the rat brains is chosen to avoid mechanical pressure.

Findings of dark neurons in connection to mobile phone exposure have been reported by Ihan et al. [60] (GSM exposure of rats for 7 days, 1 h daily). Also, an increase of oxidative damage was seen in the exposed rats as a significant increase in malondialdehyde (MDA) (an index for lipid peroxidation), nitric oxide (NO) levels, brain xanthine oxidase (XO) and adenosine deaminase (ADA) activities, as compared to the controls. With treatment of the anti-oxidant *Gingko biloba*, the EMF induced increments of XO, ADA, MDA and NO were prevented. The anti-oxidant activity of *G. biloba* is attributed to its flavinoid glycosides, which are the active compounds in the leaves. The action of these flavinoids is to destroy free radicals, such as NO and lipid peroxide radicals. Also the formation of dark neurons was reported to be prevented when the rats had been treated with *G. biloba*. Other attempts to repeat our findings of dark neurons after mobile phone exposure have been performed in a collaborative effort with Bernard Veyret's group in Bordeaux [61]. In this study, the situation 14 days and 50 days after 2 h of GSM-900 radiation exposure at average brain SAR-values of 0.14 W/kg and 2.0 W/kg was evaluated. No increased amount of dark neurons was reported.

It has been suggested that BBB leakage is the major reason for nerve cell injury, such as dark neurons in stroke-prone spontaneously hypertensive rats [62]. Albumin leaks into the brain and neuronal degeneration is seen in areas with BBB disruption in several circumstances: after intracarotid infusion of hyperosmolar solutions in rats [63]; in the stroke prone hypertensive rat [65]; in acute hypertension by aortic compression in rats [37]. The linkage between albumin extravasation over the BBB and neural damage might be a potentiating effect of albumin upon the glutamate-mediated neurotoxicity [64]. Indeed, both albumin- and glutamate-induced lesions have the same histopathological appearance with invasion of macrophages and absence of neuronal cell bodies and axons in the lesion areas [65]. The glutamate itself can also increase the BBB opening [66], leading to further albumin extravasation out into the brain parenchyma. From our previous findings of albumin extravasation 14 days after exposure [19] and dark neurons not until after 28 days [19] and 50 days [20], it could be hypothesized that albumin extravasation into the brain parenchyma, is the first observable effect of the mobile phone exposure. The albumin leakage precedes and possibly could be the cause of, the damage to the neurons seen as the dark neurons later on. In this connection, the findings of [37] that transient openings of the BBB can result in permanent tissue damage, can also be mentioned. Hypertensive opening of the BBB resulted in albumin extravasation after 2 h, but the effects remained, although to a lesser extent, also after 7 days. Many neurons with cytoplasmatic immunoreactivity for albumin appeared shrunken. Seven days after the BBB opening, there was a neuronal loss in these areas and a vigorous glial reaction, indicating that some neurons were irreversibly damaged [37].

2. Aims of the present study

In the present study we have continued to investigate the effects of EMFs upon the rat brain, now with focus on what happens 7 days after GSM exposure at 915 MHz for 2 h at non-thermal energy levels of 0.12 mW/kg, 1.2 mW/kg, 12 mW/kg and 120 mW/kg. The main questions to be answered were: whether the same increase of the BBB permeability is seen 7 days after exposure as that showed previously immediately after exposure and after 14 days, and whether different exposure levels result in a different response.

In order to compare to our previous findings, we have used the same exposure system, GSM signal, animal model and histopathological methods as in our previous studies.

3. Materials and methods

3.1. GSM exposure

The animals were exposed to RF EMFs in the same transverse electromagnetic transmission line cell (TEM-cells) as previously described and used by [1,2,5,13–19]. The TEM-cells were designed by dimensional scaling from previously constructed cells at the National Bureau of Standards [67]. TEM-cells are known to generate uniform EMFs for standard measurements.

A genuine GSM mobile phone, operating at the 900 MHz frequency band, with programmable power output, was con-

nected via a coaxial cable to the TEM-cells. Through a power splitter, the power was divided into equal parts fed into the four TEM-cells used (TEM-cell A, B, C and D). No voice modulation was applied. Each of the four TEM-cells is connected to a 50 Ω dummy load, into which the output is terminated. By using these TEM-cells, the pulse modulated exposure fields can be accurately generated without the distortion that is typically introduced when conventional antennas are used to establish impulse test fields. Thus, a relatively homogeneous exposure of the animals is allowed [68].

The TEM-cell is enclosed in a wooden box (inner dimensions of 15 cm × 15 cm × 15 cm) that supports the outer conductor, made of brass net, and central conducting plate. The central plate separates the top and bottom of the outer conductor symmetrically. Eighteen holes (diameter 18 mm) in the sidewalls and top of the wooden box make ventilation possible. Air is circulated through the holes of the TEM-cells using four fans, each placed next to the outer walls of its respective TEM-cell. The holes are also used for examination of the interior during exposure. For a further description of the TEM-cell, see [68].

The rats were placed in plastic trays (14 cm × 14 cm × 7 cm) to avoid contact with the central plate and outer conductor. The bottom of the tray was covered with absorbing paper to collect urine and faeces. Each TEM-cell contained two plastic trays, one above and one below the centre septum. Thus two rats could be kept in each TEM-cell simultaneously. All the animals could move and turn around within the TEM-cells.

For the actual experimental situation with one rat in each compartment of the TEM-cell, the conversion factor K for SAR per unit of input power could be fitted to the data as

$$K = (1.39 \pm 0.17) - (0.85 \pm 0.22)w \quad (1)$$

with w the sum of weights in kilograms of the 2 rats in the cell and the variance given as SEM. For a more detailed description, see [2].

Whole-body SAR and brain SAR vary with orientation. In our present set-up, the average of SAR for the brain grey matter was 1.06 times the average whole-body SAR, with a standard deviation of 56% around the average value for the different orientations, as estimated by us previously [19].

3.2. Animals

All animal procedures were performed according to the practices of the Swedish Board of Animal Research and were approved by the Animal Ethics Committee, Lund-Malmö.

Forty-eight inbred male and female Fischer 344 rats (the rats were supplied by Scanbur AB, Stockholm, Sweden) were 2–3 months of age at the initiation of the EMF exposure. Male and female rats weighed 225 g ± 56 g (standard deviation) and 233 g ± 60 g (standard deviation) respectively. The rats were housed in rat hutches, two in each cage, under standard conditions of 22 °C room temperature, artificial daylight illumination and rodent chow and tap water *ad libitum*.

The 48 rats were divided into four exposure groups, each group consisting of 8 rats, and one sham exposed group with 16 animals.

The peak power output from the GSM mobile phone fed into the TEM-cells was 1 mW, 10 mW, 100 mW and 1000 mW per cell respectively for a period of 2 h. This resulted in average whole-body SAR of 0.12 mW/kg, 1.2 mW/kg, 12 mW/kg and 120 mW/kg for the four different exposure groups.

All animals were kept in the animal facilities for a recovery period of 7 days after exposure. At the end of this period they were anaesthetized and sacrificed by perfusion-fixation with 4% formaldehyde.

3.3. Histopathology and methods

The brains were fixed *in situ* through saline perfusion through the ascending aorta for 3 min followed by 4% formaldehyde for 10 min and immersion in 4% formaldehyde for 24 h. They were then removed from the skulls by a non-traumatic technique (resection of bone structures at the skull base, followed by a midline incision from the foramen magnum to the nose) and immersion fixed in 4% formaldehyde for more than 24 h. Whole coronal sections of the brains were dehydrated and embedded in paraffin, sectioned at 5 μm with a microtome and stained for RNA/DNA with cresyl violet to visualize damaged neurons. Albumin was demonstrated with the IgG fraction of rabbit anti-rat albumin (Dakopatts, Helsingborg, Sweden) diluted 1:8,000. This reveals albumin as brownish spotty or more diffuse discolorations. Biotinylated swine anti-rabbit IgG was used as a secondary antibody. Then avidin, peroxidase conjugated, was coupled to the biotin and visualized with DAB (diaminobenzidine).

All brains were examined histopathologically by our neuropathologist (A.B.). All microscopic analyses were performed blind to the test situation.

Regarding albumin extravasation, the number of immunopositive extravasates (foci) were recorded under a microscope. None or occasional minor leakage was rated as normal, whereas one larger or several leakages were regarded as pathological. Immunopositive sites were, however, disregarded when localized in the hypothalamus, above the median eminence and laterally including the lateral hypothalamic nuclei, in the immediate vicinity of the third ventricle and just beneath the pial membrane. These structures are well known for their insufficient BBB. Also the presence and distribution of albumin uptake into neurons was judged semi-quantitatively.

Regarding neuronal damage, this were judged semi-quantitatively as no or occasional (score 0), moderate (score 1) or abundant occurrence (score 2) of dark neurons.

3.4. Statistics

As an initial discriminative test, the occurrence of an effect of exposure (score 1 or higher for albumin foci; score 0.5 or higher for neuronal albumin uptake and dark neurons) was tested against sham exposed controls using Fisher's exact probability test.

The Kruskal–Wallis one-way analysis of variance by ranks was used for a simultaneous statistical test of the score distributions for the five conditions of sham or EMF exposure. When the null hypothesis could be rejected, the non-parametric Mann–Whitney U-test for independent samples was used to compare each of the groups of GSM exposed and sham exposed animals.

The occurrence of covariates such as gender, the position of the rat in the TEM-cell (upper/lower compartment) and the TEM-cell used (TEM-cell A, B, C or D) was evaluated using linear regression analysis.

Spearman's non-parametric correlation analysis was used for evaluation of correlation between exposure level, albumin foci, neuronal albumin and dark neurons.

4. Results

In exposed animals there were albumin positive foci around capillaries in the white and grey matter (Fig. 5). The albumin had diffused into the neuropil between the cell bodies, surrounding the neurons, which either contained no albumin or contained albumin in some foci. Scattered neurons were albumin positive. Regarding the dark neurons, cresyl violet staining showed that these were scattered and sometimes grouped within the brain parenchyma.

The occurrence of albumin outside brain vessels was characterized as albumin foci around vessels. After the 7 days recovery time, albumin foci were found significantly more often among exposed rats (25%) than among sham exposed rats (0%) (Fisher's exact probability test, $p = 0.04$). There was a low, but significant correlation between the exposure level (SAR-value) and the occurrence of albumin foci (Spearman analysis, $r_S = 0.33$; $p = 0.04$). Taking the level of exposure and quantification of neuropathological effects into account it could be concluded from a simultaneous non-parametric comparison of all 5 exposure levels with the Kruskal–Wallis test, that the distribution of albumin foci differed significantly (Kruskal–Wallis, $p = 0.012$).

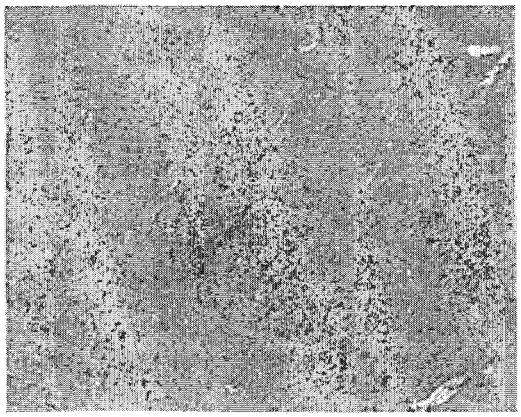


Fig. 5. Focal leakage of albumin shown in brown in the cortex. Albumin: cresyl violet, ×10. GSM-900 EMF exposure at 12 mW/kg. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Pair-wise comparisons between the different exposure levels and sham exposed animals revealed statistically significant differences for SAR of 12 mW/kg (Mann–Whitney, $p = 0.007$), whereas a trend of increased albumin extravasation could be seen for 0.12 mW/kg (Mann–Whitney, $p = 0.1$) and 120 mW/kg (Mann–Whitney, $p = 0.1$).

Also, the occurrence of neuronal albumin was evaluated. A simultaneous analysis for all exposure levels revealed a significant difference between the five groups (Kruskal–Wallis, $p = 0.03$, however Fisher's exact probability, $p =$ ns). A pair-wise comparison revealed that albumin uptake occurred more frequently at 1.2 mW/kg as compared to sham exposed (Mann–Whitney, $p = 0.02$). No difference was found for the occurrence of neuronal damage (Kruskal–Wallis, $p =$ ns; Fisher's exact probability test, $p =$ ns).

Linear regression analysis did not reveal any influence of gender, position of the animals in the TEM-cell (upper/lower compartment) or the TEM-cell used (TEM-cell A, B, C or D) on the frequency of albumin foci, neuronal albumin or occurrence of dark neurons.

5. Discussion

The present study provides evidence that GSM exposure results in disruption of the BBB permeability, with remaining, observable effects 7 days after the exposure occasion. Only non-thermal SAR-levels, below the limits of allowed exposure for humans [12] are considered. This finding of increased albumin extravasation after 7 days (Kruskal–Wallis, $p = 0.012$ with all animals included in the analysis, which is also in agreement with the Fisher's exact probability test, $p = 0.04$) is in line with our earlier findings of albumin leakage both immediately following 2 h of GSM exposure [16] and 14 days [19] after 2 h of GSM exposure. Also, the increased occurrence of neuronal albumin 7 days after the exposure is in line with the findings 14 days after exposure [19].

In our previous study, where the animals have been sacrificed immediately after the EMF exposure, we have seen albumin extravasation only at the most in 50% of the identically exposed animals, although all animals are inbred Fischer 344 rats [16]. Among the rats exposed to the pulse modulated EMFs at 915 MHz, 35% showed albumin extravasation. Also in the sham exposed animals, albumin leakage was present (in 17% of the animals). When the animals have survived 7 days after the EMF exposure, albumin extravasation is seen in a lesser proportion (25% of the exposed

animals) and in none of the sham controls. This could be due to a rapid diffusion of extravasated albumin down to, and beyond concentrations possible to demonstrate immunohistochemically. Numerous routes of clearance of extravasated molecules out from the brain tissue are present in the living brain and compounds can also become sequestered intracellularly, become protein bound or metabolized. After 14 days, albumin extravasation is seen in a somewhat larger proportion of the EMF exposed animals (29% of the exposed animals) and none of the sham controls. Thus, a secondary BBB opening might have started at some time point after the initial opening, leading to a vicious circle of albumin leakage.

The mechanism for the passage of albumin over the BBB is not clear. Extravasation might occur through paracellular routes, including alterations of tight junctions between the vascular endothelial cells, or transcellular routes with induction of pinocytosis or transcytosis, formation of transendothelial channels or disruption of the endothelial cell membrane. In connection to EMF exposure, amplified vesicle-mediated transport across the microvessel endothelium occurs, including also transendothelial channels, but no passage through disrupted inter-endothelial tight junctions [24].

One remarkable observation is that exposure at very low whole-body average power densities gives rise to a pronounced albumin leakage. In the present study, significant effects could be seen already at 12 mW/kg, although the different animal groups included a relatively small number of animals. Most certainly, the trends seen for exposure levels of 0.12 mW/kg and 120 mW/kg would have reached statistical significance if more animals had been included in the different exposure groups.

The phenomenon with increased BBB permeability already at very low energy levels might represent a U-curve response. In our other studies, we have seen that the rats in several of the groups with different SAR-levels of EMF exposure have a significant BBB opening [16,19]. The U-response curve occurs also in connection with other kinds of MW exposure, where cerebral vessel permeability after an initial rise decreased with increasing MW power [39].

Further investigation of BBB permeability in connection to EMF exposure is important not only in order to reduce the potentially harmful effects, but also to use possible beneficial effects [69]. The transport of drugs over the BBB might be regulated, so that targets within the brain can be reached. For example, steering of BBB passage of the antiretroviral agent saquinavir has been accomplished in an *in vitro* model of the human BBB, where a frequency of 915 MHz generated the highest BBB permeability [69]. This could be extremely important in order to reduce the HIV replication in the brain of HIV-infected individuals.

6. In conclusion

The time between EMF exposure and sacrifice of the animals is of great importance for the detection of albumin foci. Seven days after 2 h of GSM mobile phone exposure, there is still an increased permeability of the BBB of exposed rats. This is in concordance with earlier findings of albumin extravasation out into the brain parenchyma immediately and 14 days after 2 h of mobile phone exposure.

7. General conclusion

Taken together, it can be concluded that in a number of studies MW effects upon the BBB permeability have been observed. Increased permeability can be seen both immediately after exposure, but also 7 days after the exposure, as reported in this primary report, and after 14 days. It seems that the effects of the MW radiation might result in persistent changes, such as those seen in our own studies with neuronal damage both 28 and 50 days after 2 h of mobile phone exposure. In a future perspective, with increasing number of active mobile phone users, passive mobile phoning, radiation emitted from base stations and also MWs emitted from other communication sources, effects of low non-thermal levels of exposure must be considered further. The effects seen in the rat studies give some clues about what might possibly happen in the human brain, with a BBB very similar to that of rats. While awaiting latency periods long enough for adequate epidemiological interpretations, further studies on both animals and cells are of utmost importance.

Acknowledgements

We thank BMA Susanne Strömblad and BMA Catarina Blennow at the Rausing Laboratory for excellent technical assistance.

This work was supported by a grant from the Hans and Märit Rausing Charitable Foundation.

References

[1] L.G. Salford, B. Persson, L. Malmgren, A. Brun, in: P. Marco (Ed.), Téléphonie Mobile et Barrière Sang-Cerveau. Téléphonie mobile—effects potentiels sur la santé des ondes électromagnétiques de haute fréquence, Emburg, Belgium, 2001, pp. 141–152.

[2] H. Nittby, G. Grafström, D. Tian, A. Brun, B.R.R. Persson, L.G. Salford, J. Eberhardt, Cognitive impairment in rats after long-term exposure to GSM-900 mobile phones, Bioelectromagnetics 29 (2008) 219–232.

[3] V. Keetly, A.W. Wood, J. Spong, C. Stough, Neuropsychological sequelae of digital mobile phone exposure in humans, Neuropsychologia 44 (2006) 1843–1848.

[4] H. Lai, M.A. Carino, A. Horita, A.W. Guy, Opioid receptor subtypes that mediate a micro-wave induced decrease in central cholinergic activity in the rat, Bioelectromagnetics 13 (1992) 237–246.

[5] I.Y. Belyaev, C. Bauréus Koch, O. Terenius, K. Roxström-Lindquist, L.O.G. Malmgren, W.H. Sommer, L.G. Salford, B.R.R. Persson, Exposure of rat brain to 915 MHz GSM microwaves induces changes in gene expression but not double stranded DNA breaks or effects on chromatin conformation, Bioelectromagnetics 27 (2006) 295–306.

[6] H. Nittby, B. Widegren, M. Krogh, G. Grafström, G. Rehn, H. Berlin, J.L. Eberhardt, L. Malmgren, B.R.R. Persson, L.G. Salford, Exposure to radiation from global system for mobile communications at 1800 MHz significantly changes gene expression in rat hippocampus and cortex, Environmentalist (2008b) (published online ahead of print 15 April 2008).

[7] F. Vecchio, C. Babilono, F. Ferreri, G. Curcio, R. Fini, C. Del Percio, Maria RossiniF P., Mobile phone emission modulated interhemisperic functional coupling of EEG alpha rhythms, Eur. J. Neurosci. 25 (2007) 1908–1913.

[8] H. Hinrikus, M. Bachmann, J. Lass, D. Karai, V. Tuulik, Effect of low frequency modulated microwave exposure on human EEG: individual sensitivity, Bioelectromagnetics 29 (2008) 527–538.

[9] L. Hardell, M. Carlberg, Hansson MildF K., Case–control study on cellular and cordless telephones and the risk for acoustic neuroma or meningioma in patients diagnosed 2000–2003, Neuroepidemiology 25 (2005) 120–128.

[10] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of two case–control studies on use of cellular and cordless telephones and the risk for malignant brain tumours diagnosed in 1997–2003, Int. Arch. Occup. Environ. Health 79 (2006) 630–639.

[11] H. Nittby, G. Grafström, J.L. Eberhardt, L. Malmgren, A. Brun, B.R.R. Persson, L.G. Salford, Radiofrequency and extremely low-frequency electromagnetic field effects on the blood–brain barrier, Electromagn. Biol. Med. 27 (2008) 103–126.

[12] ICNIRP, Guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz), Health Phys. 74 (1998) 494–522.

[13] L.G. Salford, A. Brun, J. Eberhardt, L. Malmgren, B.B. Persson, Electromagnetic field-induced permeability of the blood–brain barrier shown by immunohistochemical methods. Interaction mechanism of low-level electromagnetic fields, in: B. Nordén, C. Ramel (Eds.), Living Systems, Oxford University Press, Oxford, UK, 1992, pp. 251–258.

[14] L.G. Salford, A. Brun, J.L. Eberhardt, B.R.R. Persson, Permeability of the blood–brain-barrier induced by 915 MHz electromagnetic-radiation continuous wave and modulated at 8, 16, 50 and 200 Hz, Bioelectrochem. Bioenerg. 30 (1993) 293–301.

[15] L.G. Salford, A. Brun, K. Sturesson, J.L. Eberhardt, B.R.R. Persson, Permeability of the blood–brain-barrier induced by 915 MHz electromagnetic-radiation continuous wave and modulated at 8, 16, 50 and 200 Hz, Microsc. Res. Technol. 27 (1994) 535–542.

[16] B.R.R. Persson, L.G. Salford, A. Brun, Blood–brain barrier permeability in rats exposed to electromagnetic fields used in wireless communication, Wireless Networks 3 (1997) 455–461.

[17] L.G. Salford, H. Nittby, A. Brun, G. Grafström, J.L. Eberhardt, L. Malmgren, B.R.R. Persson, Non-thermal effects of EMF upon the mammalian brain: the Lund experience, Environmentalist 27 (2007) 493–500.

[18] L.G. Salford, H. Nittby, A. Brun, G. Grafström, L. Malmgren, M. Sommarin, J. Eberhardt, B. Widegren, B.R.R. Persson, The mammalian brain in the electromagnetic fields designed by man—with special reference to blood–brain barrier function, neuronal damage and possible physical mechanisms, Prog. Theoret. Phys. Suppl. 174 (2008) 283–309.

[19] J.L. Eberhardt, B.R. Persson, A.E. Brun, L.G. Salford, L.O. Malmgren, Blood–brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones, Electromagn. Biol. Med. 27 (2008) 215–229.

[20] L.G. Salford, A. Brun, J.L. Eberhardt, L. Malmgren, B.R.R. Persson, Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones, Environ. Health. Perspect. 111 (2003) 881–883.

[21] F. Töre, P.E. Dulou, E. Haro, B. Veyret, P Aubineau, Two-hour exposure to 2-W/kg 900-MHZ GSM microwaves induces plasma protein extravasation in rat brain and dura matter, in: Proceedings of the 5th International Congress of the EBEA, Helsinki, Finland, 2001, pp. 43–45.

[22] F. Töre, P.E. Dulou, E. Haro, B. Veyret, P. Aubineau, Effect of 2 h GSM-900 microwave exposures at 2.0, 0.5 and 0.12 W/kg on plasma protein extravasation in rat brain and dura mater, in: Proceedings of the 24th Annual Meeting of the BEMS, 2002, pp. 61–62.

[23] C. Neubauer, A.M. Phelan, H. Kues, D.G. Lange, Microwave irradiation of rats at 2.45 GHz activates pinocytotic-like uptake of tracer by capillary endothelial cells of cerebral cortex, Bioelectromagnetics 11 (1990) 261–268.

[24] R.R. Shivers, M. Kavaliers, G.C. Teskey, F.S. Prato, R.M. Pelletier, Magnetic resonance imaging temporarily alters BBB permeability in the rat, Neurosci. Lett. 76 (1987) 25–31.

[25] F.S. Prato, R.H. Frappier, R.R. Shivers, M. Kavaliers, P. Zabel, D. Drost, T.Y. Lee, Magnetic resonance imaging increases the BBB permeability to 153-gadolinium diethylenetriaminepentaacetic acid in rats, Brain Res. 523 (1990) 301–304.

[26] F.S. Prato, J.M. Wills, J. Roger, H. Frappier, D.J. Drost, T.Y. Lee, R.R. Shivers, P. Zabel, BBB permeability in rats is altered by exposure to magnetic fields associated with magnetic resonance imaging at 1.5 T, Microsc. Res. Technol. 27 (1994) 528–534.

[27] G. Tsurita, H. Nagawa, S. Ueni, S. Watanabe, M. Taki, Biological and morphological effects on the brain after exposure of rats to a 1439 MHz TDMA field, Bioelectromagnetics 21 (2000) 364–371.

[28] M. Kuribayashi, J. Wang, O. Fujiwara, Y. Doi, K. Nabae, S. Tamano, T. Ogiso, M. Asamoto, T. Shirai, Lack of effects of 1439 MHz electromagnetic near field exposure on the BBB in immature and young rats, Bioelectromagnetics 26 (2005) 578–588.

[29] J.W. Finnie, P.C. Blumbergs, J. Manavis, T.D. Utteridge, V. Gebski, J.G. Swift, B. Vernon-Roberts, T.R. Kucher, Effect of global system for mobile communication (GSM)-like radiofrequency fields on vascular permeability in mouse brain, Pathology 33 (2001) 338–340.

[30] I.K. Adzamli, E.A. Jolesz, M. Blau, An assessment of BBB integrity under MRI conditions: brain uptake of radiolabelled Gd-DTPA and In-DTPA-IgG, J. Nucl. Med. 30 (1989) 839–840.

[31] E. Preston, K. Buffler, N. Haas, Does magnetic resonance imaging compromise integrity of the BBB? Neurosci. Lett. 101 (1989) 46–50.

[32] R.N. Frank, S. Dutta, M.A. Mancini, Pericyte coverage is greater in the retinal than in the cerebral capillaries of the rat, Invest. Ophthalmol. Vis. Sci. 28 (1987) 1086–1091.

[33] W.E. Thomas, Brain macrophages: on the role of pericytes and perivascular cells, Brain. Res. Rev. 31 (1999) 42–57.

[34] W.H. Oldendorf, M.E. Cornford, W.J. Brown, The large apparent work capability of the BBB: a study of the mitochondrial content of capillary endothelial cells in brain and other tissues of the rat, Ann. Neurol. 1 (1977) 409–417.

[35] A. Mihàly, B. Bozòky, Immunohistochemical localization of serum proteins in the hippocampus of human subjects with partial and generalized epilepsy and epileptiform convulsions, Acta Neuropathol. 127 (1984) 251–267.

[36] A. Mihàly, B. Bozòky, Immunohistochemical localization of extravasated serum albumin in the hippocampus of human subjects with partial and generalized and epileptiform convulsions, Acta Neuropathol. 65 (1984) 471–477.

[37] T.E.O. Sokrab, B.B. Johansson, A transient hypertensive opening of the BBB can lead to brain damage, Acta Neuropathol. 75 (1988) 557–565.

[38] A.H. Frey, S.R. Feld, B. Frey, Neural function and behaviour: defining the relationship, Ann. NY. Acad. Sci. 247 (1975) 433–439.

[39] K.J. Oscar, T.D. Hawkins, Microwave alteration of the BBB system of rats, Brain Res. 126 (1977) 281–293.

[40] J.H. Merritt, A.F. Chamness, S.J. Allen, Studies on BBB permeability, Radial. Environ. Biophys. 15 (1978) 367–377.

[41] E. Preston, R.J. Vavasour, H.M. Assenheim, Permeability of the BBB to mannitol in the rat following 2450MHz microwave irradiation, Brain Res. 174 (1979) 109–117.

[42] T.R. Ward, J.A. Elder, M.D. Long, D. Svendsgaard, Measurement of BBB permeation in rats during exposure to 2450-MHz microwaves, Bioelectromagnetics 3 (1982) 371–383.

[43] T.R. Ward, J.S. Ali, BBB permeation in the rat during exposure to low-power 1.7-GHz microwave radiation, Bioelectromagnetics 6 (1985) 131–143.

[44] S.P. Gruenau, K.J. Oscar, M.T. Folker, S.I. Rapoport, Absence of microwave effect on blood–brain-barrier permeability to [C-14]-labeled sucrose in the conscious rat, Exp. Neurol. 75 (1982) 299–307.

[45] E.N. Albert, J.M. Kerns, Reversible microwave effects on the BBB, Brain Res. 230 (1981) 153–164.

[46] H.J. Garber, W.H. Oldendorf, L.D. Braun, R.B. Lufkin, MRI gradient fields increase brain mannitol space, Magn. Reson. Imag. 7 (1989) 605–610.

[47] K. Fritze, C. Sommer, Effect of global system for mobile communication (GSM) microwave exposure on BBB permeability in rat, Acta Neuropathol. 94 (1997) 465–470.

[48] J.W. Finnie, P.C. Blumbergs, J. Manavis, T.D. Utteridge, V. Gebski, R.A. Davies, B. Vernon-Roberts, T.R. Kuchel, Effect of long-term mobile communication microwave exposure on vascular permeability in mouse brain, Pathology 34 (2002) 244–347.

[49] J.W. Finnie, P.C. Blumbergs, Z. Cai, J. Manavis, T.R. Kuchel, Effect of mobile telephony on blood–brain barrier permeability in the fetal mouse brain, Pathology 38 (2006) 63–65.

[50] T. Kumlin, H. Livonen, P. Miettinen, A. Juvonen, T. van Groen, L. Paranen, R. Pitkäaho, J. Juutilainen, H. Tanila, Mobile phone radiation and the developing brain: behavioral and morphological effects in juvenile rats, Radiat. Res. 168 (2007) 471–479.

[51] A. Schirmacher, S. Winters, S. Fischer, J. Goeke, H.J. Galla, U. Kullnick, E.B. Ringelstein, F. Stögbauer, Electromagnetic fields (1.8 GHz) increase the permeability to sucrose of the BBB in vitro, Bioelectromagnetics 21 (2000) 338–345.

[52] H. Franke, E.B. Ringelstein, F. Stögbauer, Electromagnetic fields (GSM1800) do not alter BBB permeability to sucrose in models in vitro with high barrier tightness, Bioelectromagnetics 26 (2005) 529–535.

[53] H. Franke, J. Streckert, A. Bitz, J. Goeke, V. Hansen, E.B. Ringelstein, H. Nattkämper, H.J. Galla, F. Stögbauer, Effects of universal mobile telecommunications system (UMTS) electromagnetic fields on the BBB in vitro, Radiat. Res. 164 (2005) 258–269.

[54] T. Sugimoto, G.J. Bennett, K.C. Kajander, Transsynaptic degeneration in the superficial dorsal horn after sciatic nerve injury: effects of a chronic constriction injury, transaction and strychnine, Pain 42 (1990) 205–213.

[55] Z.S. Kherani, R.N. Auer, Pharmacologic analysis of the mechanism of dark neuron production in cerebral cortex, Acta Neuropathol. 116 (2008) 447–452.

[56] D. Bexell, No neuronal apoptosis after EMF microwave exposure from mobile phones. Report supervised by Leif G. Salford at the Rausing Laboratory.

[57] E. Kövesdi, J. Pál, F. Gallyas, The fate of "dark" neurons produced by transient focal cerebral ischemia in a non-necrotic and non-excitotoxic environment: neurobiological aspects, Brain Res. 1147 (2007) 272–283.

[58] F. Gallyas, A. Csordás, A. Schwarcz, M. Mázló, "Dark" (compacted) neurons may not die through the necrotic pathway, Exp. Brain Res. 160 (2005) 473–486.

[59] B. Söderfeldt, H. Kalimo, Y. Olsson, B.K. Siesjö, Bicucullineinduced epileptic brain injury. Transient and persistent cell changes in rat cerebral cortex in the early recovery period, Acta Neuropathol. 62 (1983) 87–95.

[60] A. Ilhan, A. Gurel, F. Armutcu, S. Kamisli, M. Iraz, O. Akyol, S. Ozen, *Gingko biloba* prevents mobile phone-induced oxidative stress in rat brain, Clin. Chim. Acta 340 (2004) 153–162.

[61] F. Poulletier de Gannes, E. Haro, M. Taxile, E. Ladevze, L. Mayer, M. Lascau, P. Levêque, G. Ruffie, B. Billaudel, I. Lagroye, B. Veyret, Do GSM-900 signals affect blood–brain barrier permeability and neuron viability? in: Abstract at the 28th Annual Meeting of the Bioelectromagnetics Society, Cancun, Mexico, 2006, pp. 164–165.

[62] K. Fredriksson, H. Kalimo, C. Norberg, B.B. Johansson, Y. Olsson, Nerve cell injury in the brain of stroke-prone spontaneously hypertensive rats Acta Neuropathol. (Berl) 76 (1988) 227–237.

[63] T.S. Salahuddin, H. Kalimo, B.B. Johansson, Y. Olsson, Observations on exsudation of fibronectin, fibrinogen and albumin in the brain after carotid infusion of hyperosmolar solutions. An immunohistochemical study in the rat indicating longlasting changes in the brain microenvironment and multifocal nerve cell injuries, Acta Neuropathol. (Berl) 76 (1988) 1–10.

[64] S. Eimerl, M. Scramm, Acute glutamate toxicity in cultured cerebellar granule cells: agonist potency, effects of pH, Zn2+ and the potentiation by serum albumin, Brain Res. 560 (1991) 282–290.

[65] B. Hassel, E.G. Iversen, F. Fonnum, Neurotoxicity of albumin in vivo, Neurosci. Lett. 167 (1994) 29–32.

[66] W.D. Dietrich, O. Alonsi, M. Halley, R. Busto, M.Y.-T. Globus, Intraventricular infusion of N-methyl-D-aspartate: 1. Acute blood–brain barrier consequences, Acta Neuropathol. 84 (1992) 621–629.

[67] M.L. Crawford, Generation of Standard EM using TEM transmission cells, IEEE Trans. Electromagn. Comput. 16 (1974) 189–195.

[68] L. Malmgren, Radio frequency systems for NMR imaging: coil development and studies of non-thermal biological effects. PhD Thesis. Lund, Sweden. Department of Applied Electronics, Lund University, 1998.

[69] Y-.C. Kuo, C-.Y. Kuo, Electromagnetic interference in the permeability of saquinavir across the blood–brain barrier using nanoparticulate carriers, Int. J. Pharm. 351 (2008) 271–281.

ELSEVIER

Pathophysiology 16 (2009) 113–122

ISP PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Epidemiological evidence for an association between use of wireless phones and tumor diseases

Lennart Hardell [a,*], Michael Carlberg [a], Kjell Hansson Mild [b]

[a] *Department of Oncology, University Hospital, SE-701 85 Örebro, Sweden*
[b] *Department of Radiation Physics, Umeå University, SE-901 87 Umeå, Sweden*

Received 7 November 2008; accepted 30 January 2009

Abstract

During recent years there has been increasing public concern on potential cancer risks from microwave emissions from wireless phones. We evaluated the scientific evidence for long-term mobile phone use and the association with certain tumors in case–control studies, mostly from the Hardell group in Sweden and the Interphone study group. Regarding brain tumors the meta-analysis yielded for glioma odds ratio (OR) = 1.0, 95% confidence interval (CI) = 0.9–1.1. OR increased to 1.3, 95% CI = 1.1–1.6 with 10 year latency period, with highest risk for ipsilateral exposure (same side as the tumor localisation), OR = 1.9, 95% CI = 1.4–2.4, lower for contralateral exposure (opposite side) OR = 1.2, 95% CI = 0.9–1.7. Regarding acoustic neuroma OR = 1.0, 95% CI = 0.8–1.1 was calculated increasing to OR = 1.3, 95% CI = 0.97–1.9 with 10 year latency period. For ipsilateral exposure OR = 1.6, 95% CI = 1.1–2.4, and for contralateral exposure OR = 1.2, 95% CI = 0.8–1.9 were found. Regarding meningioma no consistent pattern of an increased risk was found. Concerning age, highest risk was found in the age group <20 years at time of first use of wireless phones in the studies from the Hardell group. For salivary gland tumors, non-Hodgkin lymphoma and testicular cancer no consistent pattern of an association with use of wireless phones was found. One study on uveal melanoma yielded for probable/certain mobile phone use OR = 4.2, 95% CI = 1.2–14.5. One study on intratemporal facial nerve tumor was not possible to evaluate due to methodological shortcomings. In summary our review yielded a consistent pattern of an increased risk for glioma and acoustic neuroma after >10 year mobile phone use. We conclude that current standard for exposure to microwaves during mobile phone use is not safe for long-term exposure and needs to be revised.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Brain tumors; Glioma; Acoustic neuroma; Meningioma; Cellular phones; Cordless phones

1. Introduction

During the last decade there has been a rapid development of wireless technology and along with that an increased use of wireless telephone communication in the world. Most persons use mobile phones and cordless phones. Additionally most populations are exposed to radiofrequency/microwave (RF) radiation emissions from wireless devices such as cellular antennas and towers, broadcast transmission towers, voice and data transmission for cell phones, pagers and personal digital assistants and other sources of RF radiation.

Concerns of health risks have been raised, primarily an increased risk for brain tumors, since the brain is the near field target organ for microwave exposure during mobile phone calls. Especially the ipsilateral brain (same side as the mobile phone has been used) is exposed, whereas the contralateral side (opposite side to the mobile phone) is much less exposed [1]. Thus, for risk analysis it is of vital importance to have information on the localisation of the tumor in the brain and which side of the head that has been predominantly used during phone calls.

Since Sweden was one of the first countries in the world to adopt this wireless technology a brief history is given in the following. First, analogue phones (NMT; Nordic Mobile Telephone System) were introduced on the market in the early 1980s using both 450 and 900 Megahertz (MHz) carrier waves. NMT 450 was used in Sweden since 1981 but closed down in December 31, 2007, whereas NMT 900 operated during 1986–2000.

* Corresponding author.
E-mail address: lennart.hardell@orebroll.se (L. Hardell).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.003

Table 1
Odds ratios (ORs) and 95% confidence intervals (CIs) from 11 case–control studies on glioma including meta-analysis of the studies. Numbers of exposed cases and controls are given.

Author, year of publication, country, reference number	No. of cases	No. of controls	OR	95% CI
Inskip et al., 2001, USA [23]	201	358	1.0	0.7–1.4
Auvinen et al., 2002, Finland [24]	Not given	Not given	1.5	1.0–2.4
Lönn et al., 2005, Sweden [25][a]	214	399	0.8	0.6–1.0
Christensen et al., 2005, low-grade glioma, Denmark [26][a]	47	90	1.1	0.6–2.0
Christensen et al., 2005, high-grade glioma, Denmark [26][a]	59	155	0.6	0.4–0.9
Hepworth et al., 2006, UK [27][a]	508	898	0.9	0.8–1.1
Schüz et al., 2006, Germany [28]	138	283	1.0	0.7–1.3
Hardell et al., 2006, Sweden [12], all glioma	346	900	1.4	1.1–1.7
Low-grade glioma	65	900	1.4	0.9–2.3
High-grade glioma	281	900	1.4	1.1–1.8
Lahkola et al., 2006, Denmark, Norway, Finland, Sweden, UK [29]	867	1 853	0.8	0.7–0.9
Hours et al., 2007, France [30]	59	54	1.2	0.7–2.1
Klaeboe et al., 2007, Norway [31][a]	161	227	0.6	0.4–0.9
Takebayashi et al., 2008, Japan [17]	56	106	1.2	0.6–2.4
Meta-analysis	>1667[b]	>3554[b]	1.0	0.9–1.1

[a] Not included in meta-analysis because already part of pooled data in Lahkola et al., 2006 [29].
[b] Total number could not be calculated since numbers were not presented in one publication [24].

The digital system (GSM; Global System for Mobile Communication) using dual band, 900 and 1800 MHz, started to operate in 1991 and now dominates the market. The third generation of mobile phones, 3G or UMTS (Universal Mobile Telecommunication System), using 1900 MHz RF broad band transmission has been introduced worldwide since a few years, in Sweden since 2003.

Desktop cordless phones have been used in Sweden since 1988, first analogue 800–900 MHz RF fields, but since early 1990s the digital 1900 MHz DECT (Digital Enhanced Cordless Telecommunications) system is used. In our studies on tumor risk associated with use of wireless phones, we have also assessed use of cordless phones. However, most other research groups have not published such data at all, or only in a scanty way, so exposure to RF from DECT is not further discussed here. Instead the reader is referred to our previous publications on this issue [2–13].

The initial studies on brain tumor risk had too short latency periods to give a meaningful interpretation. However, during recent years studies have been published that enable evaluation of ≥10-years latency period risk, although still mostly based on low numbers [14,15]. A ≥10-years latency period seems to be a reasonable minimum period to indicate long-term carcinogenic risks from exposure to RF fields during use of mobile or cordless phones.

Table 2
Odds ratios (ORs) and 95% confidence intervals (CIs) from six case–control studies on glioma including meta-analysis of the studies using ≥10 year latency period. Numbers of exposed cases and controls are given.

Study	Total			Ipsilateral			Contralateral		
Author, year of publication, country, latency, reference number	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI
Lönn et al., 2005, Sweden, ≥10 years [25][a]	25/38	0.9	0.5–1.5	15/18	1.6	0.8–3.4	11/25	0.7	0.3–1.5
Christensen et al., 2005, Denmark, low-grade glioma, ≥10 years [26][a]	6/9	1.6	0.4–6.1	–	–	–	–	–	–
Christensen et al., 2005, Denmark, high-grade glioma, ≥10 years [26][a]	8/22	0.5	0.2–1.3	–	–	–	–	–	–
Hepworth et al., 2006, UK, ≥10 years [27][a]	66/112	0.9	0.6–1.3	Not given	1.6	0.9–2.8	Not given	0.8	0.4–1.4
Schüz et al., 2006, Germany, ≥10 years [28]	12/11	2.2	0.9–5.1	–	–	–	–	–	–
Hardell et al., 2006, Sweden, >10 years [12], all glioma	78/99	2.7	1.8–3.9	41/28	4.4	2.5–7.6	26/29	2.8	1.5–5.1
Low-grade glioma	7/99	1.5	0.6–3.8	2/28	1.2	0.3–5.8	4/29	2.1	0.6–7.6
High-grade glioma	71/99	3.1	2.0–4.6	39/28	5.4	3.0–9.6	22/29	3.1	1.6–5.9
Lahkola et al., 2006, Denmark, Norway, Finland, Sweden, UK, ≥10 years [29]	143/220	0.95	0.7–1.2	77/117	1.4	1.01–1.9	67/121	1.0	0.7–1.4
Meta-analysis	233/330	1.3	1.1–1.6	118/145	1.9	1.4–2.4	93/150	1.2	0.9–1.7

[a] Not included in meta-analysis because already part of pooled data in Lahkola et al., 2006 [29].

Table 3
Odds ratios (ORs) and 95% confidence intervals (CIs) from nine case–control studies on acoustic neuroma including meta-analysis of the studies. Numbers of exposed cases and controls are given.

Author, year of publication, country, reference number	No. of cases	No. of controls	OR	95% CI
Inskip et al., 2001, USA [23]	40	358	0.8	0.5–1.4
Lönn et al., 2004, Sweden [32][a]	89	356	1.0	0.6–1.5
Christensen et al., 2004, Denmark [33][a]	45	97	0.9	0.5–1.6
Schoemaker et al., 2005, Denmark, Finland, Sweden, Norway, Scotland, England [34]	360	1934	0.9	0.7–1.1
Hardell et al., 2006, Sweden [11]	130	900	1.7	1.2–2.3
Takebayashi et al., 2006, Japan [35]	51	192	0.7	0.4–1.2
Klaeboe et al., 2007, Norway [31][a]	22	227	0.5	0.2–1.0
Schlehofer et al., 2007, Germany [36]	29	74	0.7	0.4–1.2
Hours et al., 2007, France [30]	58	123	0.9	0.5–1.6
Meta-analysis	668	3581	1.0	0.8–1.1

[a] Not included in meta-analysis because already part of pooled data in Schoemaker et al., 2005 [34].

Long-term exposure to RF fields from mobile phones and brain tumor risk is of importance to evaluate, not the least since the use of cellular phones is globally widespread with high prevalence among almost all age groups in the population. In the following we discuss mobile phone use and the association with brain tumors, but also other tumor types that have been studied. Recently, we published a detailed review of studies on brain tumors [14] followed by meta-analyses of published studies regarding glioma, acoustic neuroma and meningioma [15]. We have now recalculated these results with the addition of two new recently published articles from the Interphone study group [16,17]. Studies from individual countries were only included in the meta-analyses if they were not also included in the joint publications for several countries. For odds ratio (OR) and 95% confidence interval (CI) we used fixed effects model as in the recent publication by Kundi [18]. The analyses were done using Stata/SE 10 (Stata/SE 10 for Windows; StataCorp., College Station, TX).

One case–control study was excluded since no separate data were presented for glioma, acoustic neuroma or meningioma [19], and another since no overall data on acoustic neuroma were published, only for some time periods without results for ≥10 year latency period [20].

Due to several methodological limitations a Danish cohort study on "mobile phone subscribers" [21] is not possible to include in the meta-analysis, and the same methodological shortcomings prevail in the published updated cohort [22]. In the following only a short overview of the results for brain tumors is given, since we have discussed these issues in more detail elsewhere [14,15]. The other tumor types that have been studied are salivary gland tumors, non-Hodgkin lymphoma (NHL), testicular cancer, eye melanoma and facial nerve tumor.

2. Glioma

Glioma is a malignant type of brain tumor and comprises about 60% of all central nervous system tumors. The highly malignant glioblastoma multiform, with poor survival, is included in this group.

Eleven case–control studies present results for glioma [12,17,23–31]. Of these eight [17,25–31] were part of the Interphone study and four of these [25–27,31] were included in a pooled-analysis with additional data for Finland [29]. The results are presented in Table 1. Overall no decreased

Table 4
Odds ratios (ORs) and 95% confidence intervals (CIs) from four case–control studies on acoustic neuroma including meta-analysis of the studies using ≥10 year latency period. Numbers of exposed cases and controls are given.

Study	Total			Ipsilateral			Contralateral		
Author, year of publication, country, latency, reference number	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI
Lönn et al., 2004, Sweden, ≥10 years [32][a]	14/29	1.8	0.8–4.3	12/15	3.9	1.6–9.5	4/17	0.8	0.2–2.9
Christensen et al., 2004, Denmark, ≥10 years [33][a]	2/15	0.2	0.04–1.1	–	–	–	–	–	–
Schoemaker et al., 2005, Denmark, Finland, Sweden, Norway, Scotland, England, ≥10 years [34]	47/212	1.0	0.7–1.5	31/124	1.3	0.8–2.0	20/105	1.0	0.6–1.7
Hardell et al., 2006, Sweden, >10 years [11]	20/99	2.9	1.6–5.5	10/28	3.5	1.5–7.8	6/29	2.4	0.9–6.3
Meta-analysis	67/311	1.3	0.97–1.9	41/152	1.6	1.1–2.4	26/134	1.2	0.8–1.9

[a] Not included in meta-analysis because already part of pooled data in Schoemaker et al., 2005 [34].

or increased risk was found for glioma in the meta-analysis; OR = 1.0, 95% CI = 0.9–1.1.

Results for 10 year latency period are presented in Table 2. Six studies [12,25–29] gave such information and three [25–27] of these were also part of the publication by Lahkola et al. [29]. The meta-analysis yielded significantly increased risk for glioma with OR = 1.3, 95% CI = 1.1–1.6 increasing to OR = 1.9, 95% CI = 1.4–2.4 for ipsilateral exposure. The latter results were based on 118 exposed cases and 145 exposed controls. Regarding contralateral exposure to microwaves from mobile phones a lower risk was calculated, OR = 1.2, 95% CI = 0.9–1.7 (n = 93 cases, 150 controls). It should be noted that in the study by Takebayashi et al. [17] analyses of maximum microwave energy absorbed at the location of the tumor gave OR = 1.6, 95% CI = 0.6–4.2 related to the highest quartile of cumulative phone time weighted by maxSAR and OR = 5.8, 95% CI = 0.96–36 for subjects with cumulative maxSAR-hour of ≥10 W/kg-h.

3. Acoustic neuroma

These tumors are benign and do not undergo malignant transformation. They tend to be encapsulated and grow in relation to the auditory and vestibular portions of nerve VIII. They are slow growing tumors initially in the auditory canal, but gradually grow out into the cerebellopontine angle, where they come into contact with vital brain stem centers.

Nine case–control studies have been published [11,23, 30–36], see Table 3. Seven [30–36] were part of the Interphone study and three [31–33] were included in the publication by Schoemaker et al. [34]. Analysis of the total material yielded OR = 1.0, 95% CI = 0.8–1.1 increasing to 1.3, 95% CI = 0.97–1.9 using 10 year latency period, Table 4. For ipsilateral exposure OR increased further to 1.6, 95% CI = 1.1–2.4, whereas contralateral exposure gave a non-significantly increased risk, OR = 1.2, 95% CI = 0.8–1.9.

4. Meningioma

Meningioma arises from the pia or archnoid, which are the covering layers of the central nervous system. The majority are benign tumors that are encapsulated and well-demarched from surrounding tissue.

Regarding meningioma results have been published from nine case–control studies, Table 5 [11,16,17,23,25,26, 28,30,31]. Of these, seven [16,17,25,26,28,30,31] were part of the Interphone studies. The Lahkola et al. study [16] included three separately published Interphone studies [25,26,31]. The meta-analysis in Table 5 gave a significantly reduced OR = 0.9, 95% CI = 0.8–0.9. These results were mainly caused by the findings in the Interphone study [16] with the largest numbers of cases and controls yielding OR = 0.8, 95% CI = 0.7–0.9 in that study.

Using 10 year latency period OR was close to unity and somewhat increased for ipsilateral exposure, OR = 1.3, 95% CI = 0.9–1.8, Table 6. Regarding contralateral exposure OR was non-significantly decreased to 0.8, 95% CI = 0.5–1.3. The results for laterality were based on only two studies [11,16].

5. Brain tumor risk in different age groups

We grouped cases and controls according to age when they started to use a mobile or a cordless phone [11,12]. Consistently we found the highest risk for those with first use <20 years age. Thus, for malignant brain tumors OR = 2.7, 95% CI = 1.3–6.0 was calculated for mobile phones and OR = 2.1, 95% CI = 0.97–4.6 for cordless phones. The corresponding results for benign brain tumors were OR = 2.5, 95% CI = 1.1–5.9 and OR = 0.6, 95% CI = 0.2–1.9, respectively. Previously, we published results for diagnosis of brain tumor in different age groups [37] and found highest OR = 5.9, 95% CI = 0.6–55 for ipsilateral use of analogue phones in the youngest age group 20–29 years at the time of diagnosis. Using a >5 years latency period increased the risk further.

6. Brain tumor risk for use of mobile phone in urban and rural areas

There is a difference in output power of digital mobile phones between urban and rural areas. Adaptive power control (APC) regulates power depending on the quality of the transmission. In rural areas with on average longer distance to the base station the output power level is higher than in urban areas with dense population and shorter distance to the base stations. We studied the risk for brain tumors in urban versus rural living from the data in our study with cases diagnosed January 1, 1997 to June 30, 2000 [38]. Regarding digital phones OR = 1.4, 95% CI = 0.98–2.0 was obtained for living in rural areas increasing to OR = 3.2, 95% CI = 1.2–8.4 with >5 years latency period. The corresponding results for living in urban areas were OR = 0.9, 95% CI = 0.8–1.2 and OR = 0.9, 95% CI = 0.6–1.4, respectively.

7. Salivary gland tumors

The salivary glands, especially the parotid gland, are targets for near-field microwave exposure during calls with wireless phones. A Finnish study reported OR = 1.3, 95% CI = 0.4–4.7 for those who had ever had a mobile phone subscription [24].

Results from three case–control studies have been published, one from Sweden, one from the Nordic countries and one from Israel. During the same period as our studies on brain tumors we performed a study on salivary gland tumors [39]. Our study included the whole Swedish pop-

Table 5
Odds ratios (ORs) and 95% confidence intervals (CIs) from nine case–control studies on meningioma including meta-analysis of the studies. Numbers of exposed cases and controls are given.

Author, year of publication, country, reference number	No. of cases	No. of controls	OR	95% CI
Inskip et al., 2001 (USA) [23]	67	358	0.8	0.5–1.2
Lönn et al., 2005 (Sweden) [25][a]	118	399	0.7	0.5–0.9
Christensen et al., 2005 (Denmark) [26][a]	67	133	0.8	0.5–1.3
Schüz et al., 2006 (Germany) [28]	104	234	0.8	0.6–1.1
Hardell et al., 2006 (Sweden) [11]	347	900	1.1	0.9–1.3
Klaeboe et al., 2007 (Norway) [31][a]	96	227	0.8	0.5–1.1
Hours et al., 2007 (France) [30]	71	80	0.7	0.4–1.3
Lahkola et al., 2008 (Denmark, Norway, Finland, Sweden, UK) [16]	573	1696	0.8	0.7–0.9
Takebayashi et al., 2008, Japan [17]	55	118	0.7	0.4–1.2
Meta-analysis	1217	3386	0.9	0.8–0.9

[a] Not included in meta-analysis because already part of pooled data in Lahkola et al., 2008 [16].

ulation. Cases were recruited by using the regional cancer registries, and most had a malignant disease. They were diagnosed during 1994–2000, but with some variation for the different medical regions in Sweden. Population based controls were used as reference group. The questionnaire was answered by 267 (91%) of the cases and 750 (92%) of the controls. Of the cases 245 had a cancer diagnosis. Overall no association was found; analogue phones yielded OR = 0.9, 95% CI = 0.6–1.4, digital OR = 1.0, 95% CI = 0.7–1.5 and cordless phones OR = 1.0, 95% CI = 0.7–1.4. No effect of tumor induction period was found, although regarding >10 year latency period only 6 cases had used an analogue phone, OR = 0.7, 95% CI = 0.3–1.7, whereas no case had used a digital or cordless phone with that latency period. The results did not change significantly for ipsilateral or contralateral tumors.

The Nordic part of the Interphone case–control study of an association between use of mobile phones and parotid gland tumors was published in 2006 [40]. Detailed information about mobile phone use was obtained from 60 (85%) cases with malignant tumor, 112 (88%) with benign tumor and 681 (70%) controls. Regular mobile phone use gave OR = 0.7, 95% CI = 0.4–1.3 for malignant tumors and OR = 0.9, 95% CI = 0.5–1.5 for benign parotid gland tumors. For ipsilateral mobile phone use a latency period of ≥10 year yielded OR 0.7, 95% CI = 0.1–5.7 for malignant tumors ($n = 1$) and OR = 2.6, 95% CI = 0.9–7.9 for benign tumors ($n = 6$). Contralateral use was reported by one case with benign tumor and no case with malignant tumor in the same latency group.

As part of the Interphone study results on parotid gland tumor were reported from Israel [41]. It included 402 benign and 58 malignant incident cases, total 460 (87%) of 531 eligible for the time period 2001–2003. Population based matched controls were used, in total 1266 (66%) out of 1920 eligible subjects. Thirteen cases had a latency period of ≥10 year, which gave OR = 0.9, 95% CI = 0.4–1.8. No significantly increased risk was found for duration of use; ≥10 year yielded OR = 1.0, 95% CI = 0.5–2.1. However, for cumulative number of calls >5479 OR = 1.6, 95% CI = 1.1–2.2 was found for ipsilateral and both ears used equally, whereas contralateral use gave OR = 0.8, 95% CI = 0.5–1.2. Similarly, cumulative call time >266.3 h yielded OR = 1.5, 95% CI = 1.1–2.1; contralateral use gave OR = 0.8, 95% CI = 0.6–1.3.

In the meta-analysis using 10 year latency period no overall increased risk was found, OR = 0.8, 95% CI = 0.5–1.4, but for ipsilateral use it increased to OR = 1.7, 95% CI = 0.96–2.9, whereas contralateral use gave OR = 0.4, 95% CI = 0.2–1.2, Table 7.

Table 6
Odds ratios (ORs) and 95% confidence intervals (CIs) from five case–control studies on meningioma including meta-analysis of the studies using ≥10 year latency period. Numbers of exposed cases and controls are given.

Study	Total			Ipsilateral			Contralateral		
Author, year of publication, country, latency, reference number	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI
Lönn et al., 2005, Sweden, ≥10 years [25][a]	12/36	0.9	0.4–1.9	5/18	1.3	0.5–3.9	3/23	0.5	0.1–1.7
Christensen et al., 2005, Denmark, ≥10 years [26][a]	6/8	1.0	0.3–3.2	–	–	–	–	–	–
Schüz et al., 2006, Germany, ≥10 years [28]	5/9	1.1	0.4–3.4	–	–	–	–	–	–
Hardell et al., 2006, Sweden, >10 years [11]	38/99	1.5	0.98–2.4	15/28	2.0	0.98–3.9	12/29	1.6	0.7–3.3
Lahkola et al., 2008 (Denmark, Norway, Finland, Sweden, UK) [16]	73/212	0.9	0.7–1.3	33/113	1.1	0.7–1.7	24/117	0.6	0.4–1.03
Meta-analysis	116/320	1.1	0.8–1.4	48/141	1.3	0.9–1.8	36/146	0.8	0.5–1.3

[a] Not included in meta-analysis because already part of pooled data in Lahkola et al., 2008 [16].

Table 7
Odds ratios (ORs) and 95% confidence intervals (CIs) from three case–control studies on salivary gland tumors including meta-analysis of the studies using ≥10 year latency period.

Study	Total			Ipsilateral			Contralateral		
Author, year of publication, country, latency, reference number	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI	No. of cases/controls	OR	95% CI
Hardell et al., 2004, Sweden, >10 years [39]	6/35	0.7	0.3–1.7	5/13	1.5	0.5–4.2	1/15	0.3	0.03–2.1
Lönn et al., 2006, malignant, Sweden, ≥10 years [40]	2/36	0.4	0.1–2.6	1/23	0.7	0.1–5.7	0/19	–[a]	–[a]
Lönn et al., 2006, benign, Sweden, ≥10 years [40]	7/15	1.4	0.5–3.9	6/9	2.6	0.9–7.9	1/9	0.3	0.0–2.3
Sadetzki et al., 2007, Israel, ≥10 years [41]	13/26	0.9	0.4–1.8	10/16	1.6	0.7–3.7	3/10	0.6	0.2–2.3
Meta-analysis	28/112	0.8	0.5–1.4	22/61	1.7	0.96–2.9	5/34	0.4	0.2–1.2

[a] Not included in meta-analysis because OR could not be estimated.

8. Non-Hodgkin lymphoma

The incidence of NHL increased since the 1960s in Sweden as well as in many western countries with reliable cancer registries. This trend has levelled off since the 1990s, and decreasing exposure to environmental contaminants such as PCBs and dioxins, and also certain pesticides has been postulated to be one explanation [42,43]. As part of a large case–control study on NHL, mainly on exposure to pesticides [44], also questions on the use of wireless phones were included. The study covered the time period December 1, 1999 to April 30, 2002. The questionnaire was answered by 910 (91%) cases and 1016 (92% controls). The majority of the cases had B-cell NHL and we did not find any association with use of wireless phones [45]. Regarding T-cell NHL ($n = 53$) we observed somewhat increased risks; use of analogue phone gave OR = 1.5, 95% CI = 0.6–3.7, digital phone OR = 1.9, 95% CI = 0.8–4.8 and cordless phone OR = 2.5, 95% CI = 1.1–5.6. For certain subtypes of T-cell NHL, the cutaneous and leukemia types, the risks increased further for analogue phone to OR = 3.4, 95% CI = 0.8–15, digital phone to OR = 6.1, 95% CI = 1.3–30, and cordless phone to OR = 5.5, 95% CI = 1.3–24. These results were, however, based on low numbers.

A study from USA included 551 NHL cases and 462 frequency matched controls [46]. Among regular mobile phone users NHL risk was not significantly associated with minutes per week, duration, cumulative lifetime or years of first use. However, total time >8 years gave OR = 1.6, 95% CI = 0.7–3.8. The risk increased with number of years, and was significant for the not specified group of NHL after ≥6 years use yielding OR = 3.2, 95% CI = 1.2–8.4.

9. Testicular cancer

An increasing incidence of testicular cancer has been noted in most western countries during the recent decades. It is the most common cancer type in young men and is not regarded to be an occupational disease. Cryptorchidism is an established risk factors, but also perinatal exposure to persistent organic pollutants with hormone activity has been suggested to be another risk factor [47,48]. There has been concern in the population that use of mobile phones might be a risk factor for testicular dysfunction. We performed a case–control study mainly on the use of PVC plastics as risk factor for testicular cancer [49], and included in the questionnaire also questions on the use of wireless phones. The results were based on answers from 542 (92%) cases with seminoma, 346 (89%) with non-seminoma and 870 (89%) controls [50]. Overall no association was found [50]. Only 13 cases with seminoma had used an analogue phone >10 years yielding OR = 2.1, 95% CI = 0.8–5.1 and one case with non-seminoma; OR = 0.3, 95% CI = 0.04–2.6. No case had used a digital or cordless phone with latency period >10 years. OR did not increase with cumulative use in hours for the different phone types. Regarding use of mobile phone in the stand by mode border line significance was found for seminoma, OR = 1.3, 95% CI = 1.03–1.7, but not for non-seminoma; OR = 0.9, 95% CI = 0.7–1.3. For different localisations during stand by, highest risk was found for seminoma for keeping the phone in ipsilateral trousers pocket, OR = 1.8, 95% CI = 0.97–3.4 whereas contralateral pocket gave OR = 1.0, 95% CI = 0.5–2.0.

10. Malignant melanoma of the eye

Stang et al. [51] conducted a hospital- and population-based case–control study of uveal melanoma and occupational exposures to different sources of radiofrequency radiation. A total of 118 cases with uveal melanoma and 475 controls were included. Exposure to RF-transmitting devices was rated as (a) no RF exposure, (b) possible exposure to mobile phones, or (c) probable/certain exposure to mobile phones. An elevated risk for exposure to RF-transmitting devices was reported. Exposure to radio sets gave OR = 3.0, 95% CI = 1.4–6.3 and probable/certain exposure to mobile

phones OR = 4.2, 95% CI = 1.2–14.5. The authors concluded that several methodologic limitations prevented their results from providing clear evidence on the hypothesized association.

The study was commented among others Johansen et al. [52]. In their cohort of mobile phone subscribers in Denmark no support for an association between mobile phones and ocular melanoma was found. However, as discussed elsewhere [14,15,18,55], there are several methodological limitations in the Danish cohort [21,22] that hamper the interpretation of their findings.

The paper by Stang et al. [51] has also been commented by Inskip [53] in an editorial, the main point being that missing from the paper is any consideration of occupational or recreational exposure to UV radiation.

11. Intratemporal facial nerve tumor

So far only one investigation has studied the risk of intratemporal facial nerve (IFN) tumor and the use of mobile phone [54]. A case–control approach was used with 18 patients with IFN tumors matched with controls ($n = 192$) treated for other diseases, 51 patients treated for acoustic neuroma, 72 treated for rhinosinusitis, and 69 for dysphonia and gastroesophageal reflux. Risk of facial nerve tumorigenesis was compared by extent of mobile phone use. The OR of developing an IFN tumor was 0.6, 95% CI = 0.2–1.9 with any handheld mobile phone use and OR = 0.4, 95% CI = 0.1–2.1 for regular mobile phone use. However, they concluded that the short duration of use precludes definite exclusion as a risk for IFN tumor development. Certainly the cases were too few for a sound epidemiological study and it was not correct to include patients with acoustic neuroma in the reference group.

12. Discussion

A review on use of mobile phones and the association with brain tumors included all case–control studies that we have identified in the peer-review literature. Most studies have published data with rather short latency period and limited information on long-term users.

No other studies than from the Hardell group has published comprehensive results for use of cordless phones (DECT) [2–15]. As we have discussed in our publications it is pertinent to include also such use in this type of studies. Cordless phones are an important source of exposure to microwaves and they are usually used for a longer time period on daily basis as compared to mobile phones. Thus, to exclude such use, as was done in e.g. the Interphone studies, could lead to an underestimation of the risk for brain tumors from use of wireless phones.

We have discussed shortcomings in the Interphone studies in detail elsewhere [55]. Regarding glioma the Swedish Interphone study reported 23 ORs in Table 2 in that publication [25] and 22 of these were <1.0 and one OR = 1.0. For meningioma all 23 ORs were <1.0, six even significantly so. These results indicate a systematic bias in the study unless use of mobile phones prevents glioma and meningioma, which is biologically unlikely. It should be noted that several of the overall ORs also in other Interphone studies were <1.0, some even significantly so. As an example, in the Danish Interphone study on glioma [26] all 17 ORs for high-grade glioma were <1.0, four significantly decreased. Also other Interphone studies reported ORs significantly <1.0, that is a protective effect or rather systematic bias in the studies [16,29,31].

Use of cellular telephones was mostly assessed by personal interviews in the Interphone studies. It is not described how these personal interviews were organized, a tremendous task considering that vast parts of Sweden from north to south had to be covered. In the sparsely populated and extended area in northern Sweden personal interviews must have meant lots of long distance traveling and imposed additional stress on the interviewers. No information was given in the articles on how or if this methodological problem was solved, for example were controls only included from more densely populated areas.

The interviews in the Interphone study were extensive and computer aided. It is likely that such an interview creates a stressful situation for a patient with a recent brain tumor diagnosis and operation. These patients, especially under pressure with a newly diagnosed brain tumor and possible surgery, often have difficulties remembering past exposures and inevitably have problems with concentration and may have problems with other cognitive shortcomings. In the Danish part of the Interphone study it was concluded that the patients scored significantly lower than controls due to recalling words (aphasia), problems with writing and drawing due to paralysis [26]. According to our experience a better option would have been to start with a mailed questionnaire, that can be answered by the patient during a period of more well-being, if necessary this can be complemented by a telephone interview. After surgery it is easier to answer a questionnaire at home, also with the possibility to check phone bills to verify the use. This procedure has the additional advantage that it can be accomplished without disclosure during the data collection, whether a person is a case or a control. Certainly, knowing if it was a case or a control that was interviewed in the Interphone study may have introduced observational bias.

It has been argued that recall bias might be introduced in case–control studies on cancer patients, since the patients would be more prone to find a cause for their disease than the controls. However, the contrary is often the situation since patients do not want to blame themselves for their disease. In one article we presented data on the patients own assumptions of causes of their brain tumor [5]. Of 1429 cases only two expressed concern about mobile phones and no about cordless

phones. Interestingly, cases with a previous cancer diagnosis reported lower frequency for use of wireless phones than those with no previous cancer. No interviewer bias could be demonstrated when exposure data in the questionnaire were compared before and after phone interviews [5].

The diagnosis of tumor type as well as grading is based on histopathology. X-ray investigation or MR alone is insufficient. Of the 371 cases with glioma in the Swedish Interphone study [25] histopathology examination of the tumor was available for 328 (88%) cases, and for 225 (82%) of the meningioma cases. Thus, it is possible that cases without histology confirmation of the diagnosis may have had another type of brain tumor or even brain metastases. Such misclassifications inevitably bias the result towards unity. It is remarkable that 345 glioma cases were stratified according to grade I–IV, although histopathology was available only for 328 cases. In our studies on brain tumors we have histopathology verification of all of the diagnoses. Also, the total number of included cases [25] is not completely consistent with those reported to the Swedish Cancer Registry as we have discussed elsewhere [55]. The study included cases from neurosurgery, oncology and neurology clinics as well as regional cancer registries in the study areas.

Among the controls in the glioma and meningioma study 282 (29%) refused to participate [25]. Among some of these non-responders a short interview was made and only 34% reported regular use of a cellular telephone compared with 59% of the responders. If this discrepancy extends to the total group of non-responders the true percentage of mobile phone users in controls would be approximately 52%. Hence this figure would be lower than in glioma (58% exposed) and acoustic neuroma cases (60%). Only for meningioma with 43% exposed cases a lower percentage was reported, however, considering the sex ratio (women:men) for meningioma of about 2:1 a lower percentage of mobile phone users has to be expected due to the lower rate of users among women. It should be noted that a similar procedure in another Interphone study yielded similar results regarding mobile phone use among responders and non-responders [17].

It was discussed in a medical dissertation [56] that: 'Our Swedish study, that includes a large number of long-term mobile phone users, does not support the few previously reported positive findings, and does not indicate any risk increases neither for short-term or long-term exposures.' Considering the methodological shortcomings and that in contrast to the cited assertion of 'a large number of long-term users' the study subjects included only 25 glioma and 12 meningioma cases with long-term use, its conclusion seems to be going a long way beyond what can be scientifically defended.

It might be mentioned that this area of research seems to be controversial *per se* with unfounded statements [57], easily rebutted [58] and not supported by evolving scientific evidence [59]. Statements on no risk for brain tumors based on short-time use of mobile phones [60] might be considered in a larger context [61].

We included in our studies use of mobile or cordless phone 'any time' in the exposed group and made dose-response calculations based on number of hours of cumulative use. The unexposed group included also subjects with use of wireless phones with $\leq$1-year latency period. On the contrary, mobile phone use in the Interphone studies was defined as 'regular use' on average once per week during at least 6 months, less than that was regarded as unexposed including also all use within <1 year before diagnosis. This definition of 'regular use' seems to have been arbitrary chosen and might have created both observational and recall bias in the interpretation of such a definition.

Use of cordless phones was not assessed or not clearly presented in the Interphone studies, e.g. [25,28]. We found a consistent pattern of an association between cordless phones and glioma and acoustic neuroma [11,12]. It has been shown that the GSM phones have a median power in the same order of magnitude as cordless phones [62]. Moreover, cordless phones are usually used for longer calls than mobile phones [11,12]. Including subjects using cordless phones in the "unexposed" group in studies on this issue, as for example in the Interphone investigations, would thus underestimate the risk and bias OR against unity.

The case participation was good in our studies, 88% for cases with benign brain tumors, 90% for malignant brain tumor cases and 89% for the controls. On the contrary case participation varied from 37% to 93% and control participation from 42% to 75% in the Interphone studies. Obviously low participation rates for cases and controls might give selection bias and influence the results in the Interphone studies.

Methodological issues in the Interphone studies have been discussed elsewhere [14,15,18,55,63–65]. It was concluded that the actual use of mobile phones was underestimated in light users and overestimated in heavy users. Random recall bias could lead to large underestimation in the risk of brain tumors associated with mobile phone use. It was further suggested that selection bias in the Interphone study resulted in under selection of unexposed controls. Refusal to participate was related to less prevalent use of mobile phones, and this could result in a downward bias in estimates of the disease risk associated with mobile phone use. As discussed by Kundi [18] there was also interview lag time between cases and controls in the Interphone studies that might have been a source of bias due to the fast increase of mobile phone use during the study period. This could have resulted in underestimation of risk.

For salivary gland tumors the results were based on three case-control studies. In the 10 year latency period the meta-analysis gave an almost significantly increased risk for ipsilateral use of mobile phones, and a non-significantly decreased risk for contralateral use. These results were based on few cases. Regarding NHL and testicular cancer some subgroup analysis yielded increased risks, but these results were based on low numbers. Use of mobile phone increased the risk significantly for melanoma of the eye. The study on intratemporal facial nerve tumors is not informative since

it was based on few cases and included acoustic neuroma patients in the control group. It is concluded that all studies were hampered by low numbers of long-term users and need to be replicated for firm evidence of an association between use of mobile phones and these tumor types.

In summary our review yielded a consistent pattern of an increased risk for acoustic neuroma and glioma after >10 years mobile phone latency. Our studies showed also an association with use of cordless phones, an issue that has not been studied at all in most investigations or only rudimentary in two studies. We conclude that current standard for exposure to microwaves during mobile phone use is not safe for long-term exposure and needs to be revised.

Acknowledgements

Supported by grants from Cancer-och Allergifonden, Cancerhjälpen and Örebro University Hospital Cancer Fund. Contribution by co-workers in the various publications is acknowledged.

References

[1] E. Cardis, I. Deltour, S. Mann, M. Moissonnier, M. Taki, N. Varsier, et al., Distribution of RF energy emitted by mobile phones in anatomical structures of the brain, Phys. Med. Biol. 53 (2008) 2771–2783.

[2] L. Hardell, A. Näsman, A. Påhlson, A. Hallquist, K. Hansson Mild, Use of cellular telephones and the risk for brain tumours: a case–control study, Int. J. Oncol. 15 (1) (1999) 113–116.

[3] L. Hardell, A. Näsman, A. Påhlson, A. Hallquist, Case–control study on radiology work, medical X-ray investigations, and use of cellular telephones as risk factors for brain tumors, MedGenMed 2 (2) (2000) E2.

[4] L. Hardell, K. Hansson Mild, A. Påhlson, A. Hallquist, Ionizing radiation, cellular telephones and the risk for brain tumours, Eur. J. Cancer Prev. 10 (6) (2001) 523–529.

[5] L. Hardell, A. Hallquist, K. Hansson Mild, M. Carlberg, A. Påhlson, A. Lilja, Cellular and cordless telephones and the risk for brain tumours, Eur. J. Cancer Prev. 11 (2002) 377–386.

[6] L. Hardell, K. Hansson Mild, M. Carlberg, Case–control study on the use of cellular and cordless phones and the risk for malignant brain tumours, Int. J. Radiat. Biol. 78 (10) (2002) 931–936.

[7] L. Hardell, K. Hansson Mild, M. Carlberg, Further aspects on cellular and cordless telephones and brain tumours, Int. J. Oncol. 22 (2003) 399–407.

[8] L. Hardell, K. Hansson Mild, M. Carlberg, A. Hallquist, A. Påhlson, Vestibular schwannoma, tinnitus and cellular telephones, Neuroepidemiology 22 (2003) 124–129.

[9] L. Hardell, M. Carlberg, K. Hansson Mild, Case–control study on cellular and cordless telephones and the risk for acoustic neuroma or meningioma in patients diagnosed 2000–2003, Neuroepidemiology 25 (2005) 120–128.

[10] L. Hardell, M. Carlberg, K. Hansson Mild, Case–control study of the association between the use of cellular and cordless telephones and malignant brain tumours diagnosed during 2000–2003, Environ. Res. 100 (2) (2006) 232–241.

[11] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of two case-control studies on the use of cellular and cordless telephones and the risk of benign brain tumours diagnosed during 1997–2003, Int. J. Oncol. 28 (2006) 509–518.

[12] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of two case–control studies on use of cellular and cordless telephones and the risk for malignant brain tumours diagnosed in 1997–2003, Int. Arch. Occup. Environ. Health 79 (2006) 630–639.

[13] L. Hardell, K. Hansson Mild, M. Carlberg, F. Söderqvist, Tumour risk associated with use of cellular telephones or cordless desktop telephones, World J. Surgical Oncol. 4 (2006) 74.

[14] L. Hardell, M. Carlberg, F. Söderqvist, K. Hansson Mild, L. Lloyd Morgan, Long-term use of cellular phones and brain tumours: increased risk associated with use for ≥10 years, Occup. Environ. Med. 64 (2007) 626–632.

[15] L. Hardell, M. Carlberg, F. Söderqvist, K. Hansson Mild, Meta-analysis of long-term mobile phone use and the association with brain tumours, Int. J. Oncol. 32 (2008) 1097–1103.

[16] A. Lahkola, T. Salminen, J. Raitanen, S. Heinävaara, M. Schoemaker, H.C. Christensen, et al., Meningioma and mobile phone use—a collaborative case–control study in five North European countries. Int. J. Epidemiol. online August 2, 2008, doi:10.1093/ije/dyn155.

[17] T. Takebayashi, N. Varsier, Y. Kikuchi, K. Wake, M. Taki, S. Watanabe, et al., Mobile phone use, exposure to radiofrequency electromagnetic field, and brain tumour: a case–control study, Br. J. Cancer 98 (3) (2008) 652–659.

[18] M. Kundi, The controversy about possible relationship between mobile phone use and cancer, Environ. Health Persp. 117 (2009) 316–324.

[19] J.E. Muscat, M.G. Malkin, S. Thompson, R.E. Shore, S.D. Stellman, D. McRee, et al., Handheld cellular telephone use and risk of brain cancer, JAMA 284 (23) (2000) 3001–3007.

[20] J.E. Muscat, M.G. Malkin, R.E. Shore, S. Thompson, A.I. Neugut, S.D. Stellman, et al., Handheld cellular telephones and risk of acoustic neuroma, Neurology 58 (8) (2002) 1304–1306.

[21] C. Johansen, J. Boice, J. McLaughlin, J. Olsen, Cellular telephones and cancer—a nationwide cohort study in Denmark, J. Natl. Cancer Inst. 93 (2001) 203–207.

[22] J. Schüz, R. Jacobsen, J. Olsen, J. Boice Jr., J. McLaughlin, C. Johansen C, Cellular telephone use and cancer risk: update of a nationwide Danish cohort, J. Natl. Cancer Inst. 98 (2006) 1707–1713.

[23] P. Inskip, R. Tarone, E. Hatch, T. Wilcosky, W. Shapiro, R. Selker, et al., Cellular-telephone use and brain tumors, N. Engl. J. Med. 344 (2001) 79–86.

[24] A. Auvinen, M. Hietanen, R. Luukkonen, R. Koskela, Brain tumors and salivary gland cancers among cellular telephone users, Epidemiology 13 (2002) 356–359.

[25] S. Lönn, A. Ahlbom, P. Hall, M. Feychting, Long-term mobile phone use and brain tumor risk, Am. J. Epidemiol. 161 (2005) 526–535.

[26] H. Christensen, J. Schüz, M. Kosteljanetz, H. Poulsen, J. Boice Jr., J. McLaughlin, et al., Cellular telephones and risk for brain tumors: a population-based, incident case–control study, Neurology 64 (2005) 1189–1195.

[27] S. Hepworth, M. Schoemaker, K. Muir, A. Swerdlow, M.J.A. van Tongeren, P.A. McKinney, Mobile phone use and risk of glioma in adults: case–control study, BMJ 332 (2006) 883–887.

[28] J. Schüz, E. Böhler, G. Berg, B. Schlehofer, I. Hettinger, K. Schlaefer, et al., Cellular phones, cordless phones, and the risks of glioma and meningioma (Interphone Study Group, Germany), Am. J. Epidemiol. 163 (2006) 512–520.

[29] A. Lahkola, A. Auvinen, J. Raitanen, M. Schoemaker, H. Christensen, M. Feychting, et al., Mobile phone use and risk of glioma in 5 North European countries, Int. J. Cancer 120 (2007) 1769–1775.

[30] M. Hours, M. Bernard, L. Montestrucq, M. Arslan, A. Bergeret, I. Deltour, et al., Cell phones and risk of brain and acoustic nerve tumours: the French INTERPHONE case–control study, Rev. Epidemiol. Sante Publique 55 (2007) 321–332.

[31] L. Klaeboe, K. Blaasaas, T. Tynes, Use of mobile phones in Norway and risk of intracranial tumours, Eur. J. Cancer Prev. 16 (2007) 158–164.

[32] S. Lönn, A. Ahlbom, P. Hall, M. Feychting, Mobile phone use and the risk of acoustic neuroma, Epidemiology 15 (2004) 653–659.

[33] H. Christensen, J. Schüz, M. Kosteljanetz, H. Poulsen, J. Thomsen, C. Johansen, Cellular telephone use and risk of acoustic neuroma, Am. J. Epidemiol. 159 (2004) 277–283.
[34] M. Schoemaker, A. Swerdlow, A. Ahlbom, A. Auvinen, K. Blaasaas, E. Cardis, et al., Mobile phone use and risk of acoustic neuroma: results of the Interphone case–control study in five North European countries, Br. J. Cancer 93 (2005) 842–848.
[35] T. Takebayashi, S. Akiba, Y. Kikuchi, M. Taki, K. Wake, S. Watanabe, et al., Mobile phone use and acoustic neuroma risk in Japan, Occup. Environ. Med. 63 (2006) 802–807.
[36] B. Schlehofer, K. Schlaefer, M. Blettner, G. Berg, E. Böhler, I. Hettinger, et al., Environmental risk factors for sporadic acoustic neuroma (Interphone Study Group, Germany), Eur. J. Cancer 43 (2007) 1741–1747.
[37] L. Hardell, K. Hansson Mild, M. Carlberg, A. Hallquist, Cellular and cordless telephones and the association with brain tumours in different age group, Arch. Environ. Health 59 (3) (2004) 132–137.
[38] L. Hardell, K. Hansson Mild, M. Carlberg, Use of cellular telephones and brain tumour risk in urban and rural areas, Occup. Environ. Med. 62 (2005) 390–394.
[39] L. Hardell, A. Hallquist, K. Hansson Mild, M. Carlberg, H. Gertzén, E. Schildt, et al., No association between the use of cellular or cordless telephones and salivary gland tumours, Occup. Environ. Med. 61 (8) (2004) 675–679.
[40] S. Lönn, A. Ahlbom, H. Christensen, C. Johansen, J. Schüz, S. Edström, et al., Mobile phone use and risk of parotid gland tumor, Am. J. Epidemiol. 164 (7) (2006) 637–643.
[41] S. Sadetzki, A. Chetrit, A. Jarus-Hakak, E. Cardis, Y. Deutch, S. Duvdevani, et al., Cellular phone use and risk of benign and malignant parotid gland tumors—a nationwide case–control study, Am. J. Epidemiol. 167 (4) (2008) 457–467.
[42] L. Hardell, M. Eriksson, Is the decline of the increasing incidence of non-Hodgkin lymphoma in Sweden and other countries a results of cancer preventive measures? Environ. Health Perspect. 111 (2003) 1704–1706.
[43] L. Hardell, Pesticides, soft-tissue sarcoma and non-Hodgkin lymphoma—historical aspects on the precautionary principle in cancer prevention, Acta Oncol. 47 (3) (2008) 347–354.
[44] M. Eriksson, L. Hardell, M. Carlberg, M. Åkerman, Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis, Int. J. Cancer 123 (2008) 1657–1663.
[45] L. Hardell, M. Eriksson, M. Carlberg, C. Sundström, K. Hansson Mild, Use of cellular or cordless telephones and the risk for non-Hodgkin's lymphoma, Int. Arch. Occup. Environ. Health 78 (8) (2005) 625–632.
[46] M.S. Linet, T. Taggart, R.K. Severson, J.R. Cerhan, W. Cozen, et al., Cellular telephones and non-Hodgkin lymphoma, Int. J. Cancer 119 (2006) 2382–2388.
[47] L. Hardell, B. van Bavel, G. Lindström, M. Carlberg, A.C. Dreifaldt, H. Wijkström, et al., Increased concentrations of polychlorinated biphenyls, hexachlorobenzene and chlordanes in mothers to men with testicular cancer, Environ. Health Perspect. 111 (2003) 930–934.
[48] L. Hardell, B. van Bavel, G. Lindström, M. Eriksson, M. Carlberg, In utero exposure to persistent organic pollutants in relation to testicular cancer, Int. J. Androl. 29 (2006) 228–234.
[49] L. Hardell, N. Malmqvist, C.G. Ohlson, H. Westberg, M. Eriksson, Testicular cancer and occupational exposure to polyvinyl chloride plastics: a case–control study, Int. J. Cancer 109 (2004) 425–429.
[50] L. Hardell, M. Carlberg, C.G. Ohlson, H. Westberg, M. Eriksson, K. Hansson Mild, Use of cellular and cordless telephones and risk of testicular cancer, Int. J. Androl. 30 (2) (2007) 115–122.
[51] A. Stang, G. Anastassiou, W. Ahrens, K. Bromen, N. Bornfeld, K. Jöckel, The possible role of radiofrequency radiation in the development of uveal melanoma, Epidemiology 12 (2001) 7–12.
[52] C. Johansen, J.D. Boice Jr., J.K. McLaughlin, H.C. Christensen, J.H. Olsen, Mobile phones and malignant melanoma of the eye, Br. J. Cancer 86 (2002) 348–1348.
[53] P.D. Inskip, Frequent radiation exposures and frequency dependent effects: the eyes have it. (Editorials), Epidemiology 12 (2001) 1–4.
[54] H. Warren, A. Prevatt, K. Daly, P. Antonelli, Cellular telephone use and risk of intratemporal facial nerve tumor, Laryngoscope 113 (2003) 663–667.
[55] L. Hardell, M. Carlberg, K. Hansson Mild, Methodological aspects of epidemiological studies on the use of mobile phones and their association with brain tumors, Open Environ. Sci. 2 (2008) 54–61.
[56] S. Lönn, Mobile phone use and risk of intercranial tumors, Medical Dissertation, Karolinska Institute, Stockholm, Sweden, 2004.
[57] H.O. Adami, A. Ahlbom, A. Ekbom, L. Hagmar, M. Ingelman-Sundberg, Opinion—"Experts who talk rubbish", Bioelectromag. Soc. Newslett. 162 (2001) 4–5.
[58] L. Hardell, M. Walker, B. Walhjalt, L.S. Friedman, E.D. Richter, Secret ties to industry and conflicting interests in cancer research, Am. J. Ind. Med. 50 (2007) 227–233.
[59] Risk evaluation of potential environmental hazards from low frequency electromagnetic field exposure using sensitive *in vitro* methods. Final Report, Available from: <http://www.itis.ethz.ch/downloads/REFLEX_Final%20Report_171104.pdf>.
[60] D. Trichopoulus, H.O. Adami, Cellular telephones and brain tumors, N. Engl. J. Med. 344 (2) (2001) 133–134.
[61] D. Michaels, Doubt is Their Product. How Industry's Assault on Science Threatens Your Health, Oxford University Press, New York, 2008.
[62] K. Hansson Mild, L. Hardell, M. Kundi, M.O. Mattsson, Mobile phones and cancer: is there really no evidence of an association? (Review), Int. J. Mol. Med. 12 (2003) 67–72.
[63] M. Vrijheid, E. Cardis, B. Armstrong, A. Auvinen, G. Berg, K. Blaasaas, et al., Validation of short term recall of mobile phone use for the Interphone study, Occup. Environ. Med. 63 (4) (2006) 237–243.
[64] M. Vrijheid, I. Deltour, D. Krewski, M. Sanchez, E. Cardis, The effects of recall errors and of selection bias in epidemiologic studies of mobile phone use and cancer risk, J. Expo. Sci. Environ. Epidemiol. 16 (4) (2006) 371–384.
[65] M. Vrijheid, L. Richardson, B.K. Armstrong, A. Auvinen, G. Berg, M. Carrol,1, et al., Quantifying the impact of selection bias caused by non-participation in a case–control study of mobile phone use, Annals Epidemiol. 19 (2009) 33–41.

ELSEVIER

Pathophysiology 16 (2009) 123–135

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Mobile phone base stations—Effects on wellbeing and health

Michael Kundi *, Hans-Peter Hutter

Institute of Environmental Health, Center for Public Health, Medical University of Vienna, Kinderspitalgasse 15, A-1095 Vienna, Austria

Received 11 September 2008; accepted 30 January 2009

Abstract

Studying effects of mobile phone base station signals on health have been discouraged by authoritative bodies like WHO International EMF Project and COST 281. WHO recommended studies around base stations in 2003 but again stated in 2006 that studies on cancer in relation to base station exposure are of low priority. As a result only few investigations of effects of base station exposure on health and wellbeing exist. Cross-sectional investigations of subjective health as a function of distance or measured field strength, despite differences in methods and robustness of study design, found indications for an effect of exposure that is likely independent of concerns and attributions. Experimental studies applying short-term exposure to base station signals gave various results, but there is weak evidence that UMTS and to a lesser degree GSM signals reduce wellbeing in persons that report to be sensitive to such exposures. Two ecological studies of cancer in the vicinity of base stations report both a strong increase of incidence within a radius of 350 and 400 m respectively. Due to the limitations inherent in this design no firm conclusions can be drawn, but the results underline the urgent need for a comprehensive investigation of this issue. Animal and in vitro studies are inconclusive to date. An increased incidence of DMBA induced mammary tumors in rats at a SAR of 1.4 W/kg in one experiment could not be replicated in a second trial. Indications of oxidative stress after low-level in vivo exposure of rats could not be supported by in vitro studies of human fibroblasts and glioblastoma cells.

From available evidence it is impossible to delineate a threshold below which no effect occurs, however, given the fact that studies reporting low exposure were invariably negative it is suggested that power densities around 0.5–1 mW/m^2 must be exceeded in order to observe an effect. The meager data base must be extended in the coming years. The difficulties of investigating long-term effects of base station exposure have been exaggerated, considering that base station and handset exposure have almost nothing in common both needs to be studied independently. It cannot be accepted that studying base stations is postponed until there is firm evidence for mobile phones.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Mobile phone base station; Performance; Cancer; In vitro studies; Microwaves

1. Introduction

Modern mobile telecommunication is based on a cellular system. Each cell is covered by a base station that keeps track of the mobile phones within its range, connects them to the telephone network and handles carry-over to the next base station if a customer is leaving the coverage area. Early mobile telecommunication systems had very large cells with tens of kilometers radius and were predominantly located along highways due to offering service mainly for car-phones. With the introduction of digital mobile phone systems cell sizes got much smaller and base stations were erected in densely populated areas. The limited power of mobile phones made it necessary to reduce the distance to the customers. The cell size depends on (1) the radiation distance of the mobile phone; (2) the average number of connected calls; (3) the topographic characteristics of the covered area and the surrounding buildings, vegetation and other shielding objects; and (4) the type of antenna used. There are essentially three types of cells presently making up mobile telecommunication networks: (1) macro-cells in areas of average to low number of calls; (2) micro-cells in densely populated areas and areas with high telecommunication traffic density; (3) pico-cells within buildings, garages, etc. The types of antennas used, although hundreds of different models are operated, can be subdivided into: omni-directional antennas that radiate in all horizontal directions with the same power; sector antennas

* Corresponding author. Tel.: +43 1 4277 64726; fax: +43 1 4277 9647.
E-mail address: michael.kundi@meduniwien.ac.at (M. Kundi).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.008

that radiate the main beam in one sector only but have varying aperture (usually 120° or 90°). These antennas can be mounted on masts (that sometimes are in the shape of trees for protection of landscape or are otherwise hidden), on the top of buildings, on pylons, and micro- and pico-cell antennas on various other places (walls of houses, shops, indoors, etc.). The width of the beam in vertical direction is typically 6°, but due to the presence of side lobes the actual pattern is more complicated.

Digital base stations of the second generation (GSM, TDMA) and third generation (UMTS, CDMA) have typically a nominal power for each channel of 10–20 W, micro- and pico-cells up to about 4 and 2 W, respectively. Due to the antenna gain the EIRP in the direction of the main beam is much greater (by a factor of $10^{g/10}$, where g is the antenna gain in dB, typically between 40 and 60). Most base stations of the second generation operate with two channels, one broadcast control channel (BCCH, channel used for transmitting information about the network, the location area code, frequencies of neighboring cells, etc.) and one traffic channel (TCH, channel used for transmission of calls), for third generation systems, due to code division multiplexing, control information needed for the maintenance of the system is at present transmitted together with the actual information (calls, pictures, etc.) within one broad-band channel. GSM systems operate the BCCH with all time slots occupied and therefore at maximal power, whereas TCH has as many time slots active as necessary to operate all active transmission not covered by the BCCH. Field strength at ground level depends on the characteristics of the antenna. Because the main beam reaches ground level typically in 50–200 m distance, in case of free sight to the antenna, maximum field strength is reached at that distance. However, due to the side lobes ups and downs of field strength occur as one approach the base station. In areas where objects are shadowing the beams, patterns are still more complex because of diffraction and reflection and multi-path propagation with constructive as well as destructive interference.

Free field propagation from the antenna along the main beam follows the law: $P(x) = \mathrm{EIRP}/(4\pi \cdot x^2)$, with $P(x)$ the power flux density in x meters distance and EIRP the equivalent isotropic radiated power of the antenna. Significant deviations from this expectation occur due to the side lobes, presence of interfering objects, differences in vertical beam width, and variations in the number of active transmissions. For these reasons distance to the antenna is a poor proxy for exposure level.

Since the early 1990s tens of thousands of base stations have been erected in countries where digital networks were introduced. While older systems with their low number of base stations have hardly received public attention, the vast increase in base stations has led to public concerns all over the world. Anecdotal reports about various effects on wellbeing and health have led also to an increased awareness of physicians [1,2] and increased research efforts have been demanded [3]. Despite these professional and public concerns, the WHO International EMF Project has discouraged research into effects of base stations, because it deemed research into effects of mobile phones of higher priority. This position was changed in 2003 when the new research agenda recommended studies around base stations. In 2006 it was again stated that research into potential health effects of base station is of low priority [4].

Due to these circumstances only very few investigations of effects of base stations on wellbeing and health exist. In addition some experimental studies have been conducted, most of which address the problem of short-term effects on complaints and performance.

The following review summarizes available evidence and critically assesses the investigations as to their ability to support or dismiss a potential effect of microwave exposure from base stations on wellbeing and health.

2. Epidemiological investigations

2.1. Wellbeing and performance

Santini et al. [5,6] report results of a survey in France to which 530 individuals (270 men and 260 women) responded. Study subjects were enrolled through information given by press, radio, and website, about the existence of a study on people living near mobile phone base stations. Frequency for each of 18 symptoms was assessed on a 4 level scale (never, sometimes, often, and very often). Participants estimated distance to the base station using the following categories: <10 m, 10–50 m, 50–100 m, 100–200 m, 200–300 m, >300 m. For comparison of prevalence of symptoms >300 m served as reference category. For all symptoms a higher frequency of the categories 'often' or 'very often' was found at closer (self-reported) distance to the base station. Fatigue, headaches, and sleeping problems showed highest relative increase. Due to a less than optimal statistical analysis comparing each distance category separately with the reference category the overall response pattern can only be assessed qualitatively. Fig. 1 shows relative prevalence averaged over all symptoms as a function of self-reported distance to the antenna. Interestingly the function is not monotonous but shows, after an initial drop, an increase at a distance of 50–100 m. Because of the fact that in many cases this is the distance at which the main beam reaches ground level this may indicate a relationship to actual exposure levels.

This study was a first attempt to investigate a potential relationship between exposure to base station signals and health and has, therefore, several shortcomings: (1) participants selected themselves into the study group by responding to public announcements; (2) distance was self-reported and no attempt was made to validate these reports (a German cross-sectional study in over 30,000 households revealed that more than 40% did not know they were living in the vicinity of a base station [7]); (3) no assessment of subjects' concerns about the base station; and (4) no measurement or calcula-

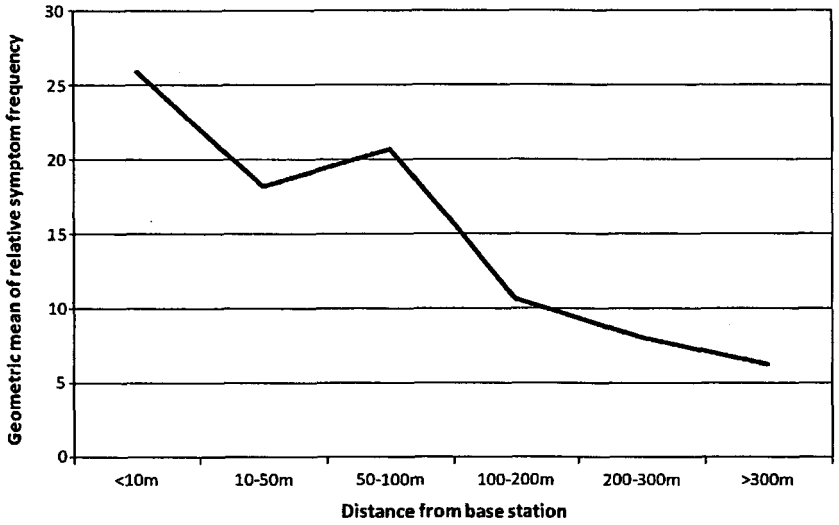


Fig. 1. Relative symptom frequency averaged over all 33 reported symptoms from Santini et al. [5] as a function of distance from base station.

tion of actual exposure. Although selection bias and wrong estimation of distance to the base station could have led to a spuriously increased prevalence of symptoms, the pattern of symptom frequency as a function of distance is intriguing and suggests that part of the increased symptom prevalence could be due to exposure because people do not know the typical pattern of field strengths found in the vicinity of base stations.

A Spanish version of the questionnaire as applied in the French study was distributed in La Nora, a small town in Murcia, Spain, to about 145 inhabitants [8]. Overall 101 questionnaires (from 47 men and 54 women) were included in the analyses. Electric field strength in the frequency range 1 MHz to 3 GHz was measured in the bedrooms of the participants. Data were analyzed in two different ways: first subjects were subdivided into those living less than 150 m from the base station and a second group living more than 250 m away (according to self-reports); the average exposure level of the first group was 1.1 mW/m^2, and of the second group 0.1 mW/m^2; self-reported symptom severity was compared across these groups. The second method correlated log transformed field strengths with symptom scores. The majority of symptoms showed a relationship both by comparison of the contrast groups according to distance from the base station as well as when correlated to measured field strength. Strongest effects were observed for headaches, sleep disturbances, concentration difficulties, and discomfort.

In contrast to the French investigation the study has assessed actual exposure by short-term measurements in the bedrooms of participants. The fact that both, reported distance as well as measured field strength, correlated with symptom severity supports the hypothesis of an association between microwaves from the base station and wellbeing. However, because subjects knew that the intention of the study was to assess the impact of the base station there is a potential for bias. Also concerns of the participants about effects of the base station on health were not assessed. Furthermore, method of selection of participants was not reported.

In a cross-sectional study in the vicinity of 10 GSM base stations in rural and urban areas of Austria, Hutter et al. [9] selected 36 households randomly at each location based on the characteristics of the antennas. Selection was done in such a way as to guarantee a high exposure gradient. Base stations were selected out of more than 20 locations based on the following criteria: (1) at least 2 years operation of the antenna; (2) no protest against it before or after erection; (3) no nearby other base station; (4) transmission only in the 900 MHz frequency band. (The last two criteria were not fully met in the urban area.) In order to minimize intervention of interviewers all tests and questionnaires were presented on a laptop computer and subjects fulfilled all tasks on their own. Wellbeing was assessed by a symptoms list (v. Zerssen scale), sleeping problems by the Pittsburgh sleeping scale. In addition several tests of cognitive performance were applied. Concerns about environmental factors were inquired and sources of EMF exposure in the household were assessed as well. It was not disclosed to the subjects that the study was about the base station, but about environmental factors in general. Among other measurements high-frequency fields were assessed in the bedrooms. From the measured field strength of the BCCH maximum and minimum exposure to the base station signals were computed. In addition overall power density of all high-frequency fields was measured. Results of measurements from 336 households were available for analysis. Exposure from the base station was categorized into three ranges: below 0.1 mW/m^2, between 0.1 and 0.5 mW/m^2, and above 0.5 mW/m^2. Cognitive performance tended to be better at higher exposure levels and was statistically significant for perceptual speed after correction for confounders (age, gender, mobile phone use, and concerns about the base station). Subjective symptoms were generally more frequent at higher exposure levels and statistically increased prevalence was found for headaches, cold hands or feet, and concentration difficulties. Although participants reported more sleeping problems at higher exposure

levels, this effect was removed after controlling for concerns about the base station.

Despite limitations inherent in the cross-sectional study design the methodological problems mentioned in the French and Spanish investigations were avoided. Authors conclude: "The results of this study indicate that effects of very low but long lasting exposures to emissions from mobile telephone base stations on wellbeing and health cannot be ruled out. Whether the observed association with subjective symptoms after prolonged exposure leads to manifest illness remains to be studied."

A study in employees working within or opposite a building with GSM base station antennas on the roof was reported by Abdel-Rassoul et al. [10]. The investigation took place in Shebin El-Kom City, Menoufiya Governorate, Egypt, where the first mobile phone base station was erected in 1998 on a building for agricultural professions. Overall 37 subjects working within this building and 48 subjects working in the agricultural directorate about 10 m opposite the building were considered exposed. A control group, working in another building of the agricultural administration located approximately 2 km away, consisted of 80 persons. Participants completed a structured questionnaire assessing educational and medical history. A neurological examination was performed and a neurobehavioral test battery (tests for visuomotor speed, problem solving, attention and memory) was presented. The combined exposed groups were compared to the control group that was matched by sex, age and other possible confounders. Statistical analysis accounted for these variables. Further comparisons were performed between subjects working in the building with the base station on the roof and those opposite. Exposed subjects performed significantly better in two tests of visuomotor speed and one test of attention, in two other tests the opposite was the case. The prevalence of headaches, memory problems, dizziness, tremors, depressive symptoms, and sleep disturbances was significantly higher among exposed inhabitants than controls. Measurements conducted 3 years before the investigation revealed compliance with the Egyptian standard (80 mW/m^2) with values between 27 and 67 mW/m^2, but locations of the measurements were not specified.

Like in the study of Hutter et al. [9] it was not disclosed to the participants that the study was about the base station. An important aspect is studying employees that occupy the area of exposure for 8–16 h a day. Several possible confounders (age, sex, education, smoking, and mobile phone use) were considered and did not change the reported results. Other factors like stressful working conditions, indoor pollutants and other attributes of the work place were not assessed and might have had an effect on the reported symptoms. Although no recent measurements were available it can be assumed that both, subjects working within the building as well as those opposite the building with the base station are exposed at comparatively high levels. The picture of one antenna shown in the article indicates that the panel is slightly uptilted. It can be assumed that the sidelobes of the antenna are directed downwards into the building below the base station as well as into the opposite building. Measurements in Germany revealed that, in contrast to a general belief that there is no significant exposure in buildings below a base station antenna, the field strength in buildings below an antenna is almost equal to field strength in opposite buildings.

An experimental field trial was conducted in Bavaria [11] during three months before an UMTS antenna on a governmental building started operation. Based on a random sequence the antenna was turned on or off one, two, or three days in a row during 70 working days in winter 2003. Conditions were double-blind since neither the experimenters nor the participants knew whether the antenna was on or off. This was guaranteed by software manipulation of the antenna output that prohibited UMTS mobile phones from contacting the base station and by locating the computer controlling the antenna in a sealed room. The UMTS antenna operated at a mean frequency of 2167.1 MHz. The protocol has not been specified, but considering that no real transmission occurred it is assumed that only the service channel was used. The antenna had a down-tilt of 8° expected to result in rather high exposure within the building. Measured electric field strength in the rooms of the participants varied between the detection limit of the field probe (0.05 V/m) and 0.53 V/m (corresponding to 0.75 mW/m^2) with an average of 0.10 ± 0.09 V/m (corresponding to 0.03 mW/m^2). Participants should answer an online questionnaire on each working day they were in the office in the morning when they arrived and in the evening shortly before leaving. The questionnaire consisted of a symptom list with 21 items, and in the evening participants should state whether or not they considered the antenna has been on during this day and whether they considered, if they experienced any adverse effects, these effects due to the base station. From approximately 300 employees working in the building 95 (28 females, 67 males) that answered the questionnaire on at least 25% of the working days were included in the analysis.

None of the 21 symptoms showed a statistically significant difference between days on and days off. A more comprehensive analysis of the overall score across all 21 items applying a mixed model with subjects as random factor and autoregressive residuals revealed a tendency ($p = 0.08$) for an effect of actual exposure on the difference between morning and evening values. Self-rated electrosensitivity had a significant effect on evening scores but did not affect difference scores. As expected, subjective rating of exposure had a significant influence both, on evening scores and score difference. Correct detection rate of base station transmission mode was 50% and thus equal to chance. No person was able to detect operation mode correctly on significantly more days than expected.

The study design was a great strength of this pilot investigation. It combined the advantages of a field trial with the rigorous control of exposure conditions in an experiment. However, there are a number of severe shortcomings too: first, no correction for actual exposure has been applied. As

stated above, exposure varied considerably within the building and some participants were not exposed at detectable levels at all. The resulting exposure misclassification leads to a bias towards the null hypothesis. Furthermore, it was not specified which UMTS protocol was actually transmitted. Another important limitation is the quite low exposure even in the offices with the highest levels. Problems with the statistical evaluation are indicated by a highly significant time factor suggesting insufficient removal of autocorrelation. Finally, the symptom list contains several items that were not implicated previously as related to exposure from base stations (e.g. back pain). Such items reduce the overall power to detect an effect of base station exposure.

A cross-sectional study based on personal dosimetry was conducted in Bavaria [12]. In a sample of 329 adults (173 females, 155 males, and 1 unknown) chronic and acute symptoms were assessed. Chronic symptoms were taken from the Freiburger Beschwerdeliste and acute symptoms from the v. Zerssen list. Symptoms assessed were headache, neurological symptoms, cardiovascular symptoms, concentration problems, sleeping disorders and fatigue. Participants wore a dosimeter (Maschek ESM 140) for 24 h on the upper arm on the side used for holding a phone (during the night the dosimeter was placed next to the bed). The dosimeter measured exposure in frequency bands including GSM 900 up- and down-link, GSM 1800 up- and down-link, UMTS, DECT and WLAN (2.45 GHz).

Acute symptoms at noon and in the evening were dichotomized and related to exposure during the previous 6 h (night time measurements were considered biased and not analyzed). Exposure was expressed in percent of the ICNIRP reference levels. Odds ratios for the different symptom groups were computed in relation to exposure subdivided into quartiles with the first quartile as reference. Similarly, dichotomized chronic symptoms were related to average day time exposure levels. None of the symptom groups was significantly related to exposure. Odds ratios for headaches and cardiovascular symptoms during the last 6 months were increased for all three tested exposure quartiles (for headaches odds ratios were: 1.7, 2.7, and 1.2 for 2nd to 4th quartile; for cardiovascular symptoms these figures were 1.4, 3.3, and 2.4). But none of these odds ratios was statistically significant. Acute symptoms at noon and in the evening showed a tendency for lower prevalence of fatigue at higher exposure levels. Odds ratios for headaches and concentration problems in the evening were increased at higher exposure levels in the afternoon but also these results were statistically not significant (odds ratios for headaches were 1.7, 1.6, 3.1 and for concentration problems 1.4, 2.0, 1.4 for 2nd to 4th quartile of afternoon exposure levels).

Exposure was low and ranged from a daytime average of 0.05 V/m (at or below the limit of determination) to 0.3 V/m (corresponding to 0.24 mW/m^2 power density). (In order to make results comparable to other investigations figures expressed in percent of ICNIRP reference levels were recalculated to field strengths and power densities). Quartiles for daytime exposure were: up to 0.075 V/m, 0.075 to 0.087 V/m, 0.087 to 0.110 V/m, and 0.110 to 0.3 V/m. It can be seen that the first three quartiles are almost indiscernible with a ratio of the upper limit of the third and first quartiles of only 1.5.

Although the study of Thomas et al. [12] was the first one using personal dosimetry in the context of investigating effects of exposure to mobile phone base station signals on wellbeing it has not explored the potential of an almost continuous exposure measurement. Only average exposure was computed and the probably most important nighttime values were left out. A number of different exposure metrics should have been assessed, like duration of exposure above a certain limit, maximum exposure level, longest period below limit of determination, and variability of exposure levels to name but a few. Furthermore, prevalence of symptoms was so low that the power of the investigation to detect even substantially increased risks was inferior (less than 25%). Despite these shortcomings the study has its merits as a first step in using personal dosimetry. An earlier report of the group [13] with a comparison between two personal dosimeters (Maschek and Antennessa) demonstrated that improvements are necessary before personal dosimetry can be successfully used in epidemiological studies.

A large population-based cross-sectional study was conducted in the context of the German 'Mobile Phone Research Program' in two phases [7]. In the initial phase 30,047 persons from a total of 51,444 (58% response rate) who took part in a nationwide survey also answered questions about mobile phone base stations. Additionally a list of 38 health complaints (Frick's list) was answered. Distance to the nearest base station was calculated based on geo-coded data of residences and base stations. In the second phase, all respondents (4150 persons) residing in eight preselected urban areas were contacted. In total, 3526 persons responded to a postal questionnaire (85% response rate) including questions about health concerns and attribution of symptoms to exposures from the base station as well as a number of standardized questionnaires: the Pittsburgh Sleep Quality Index, the Headache Impact Test, the v. Zerssen list of subjective symptoms, the profile of mental and physical health (SF 36), and a short version of the Trier Inventory of Chronic Stress. Overall 1808 (51%) of those that responded to the questionnaire agreed to have EMF measurement taken in their homes. Results of the large survey from the first phase of the study revealed a fraction of 10% of the population who attributed adverse health effects to the base station. An additional 19% were generally concerned about adverse effects of mobile phone base stations. Regression analysis of the symptoms summary score on distance to the base station (less or more than 500 m) and attribution/concerns about adverse effects adjusted for possible confounders (age, gender, SES, region and size of community) revealed a small but significant increase of the symptom score at closer distance to the base station. Higher effects, however, were obtained for concerns about adverse effects of the base station (with higher scores for those concerned) and still higher effects for

those that attributed their health problems to exposures from mobile phone base stations. The latter result is only to be expected because attribution presupposes existence of symptoms and hence those with attribution must have higher scores than those without. Because effects of concerns/attribution were accounted for in the multivariate model, effect of distance to the base station is independent of these concerns or attributions. In the second phase measurements in the bedrooms revealed an overall quite low exposure to EMFs from the base station. Only in 34% of the households was the exposure above the sensitivity limit of the dosimeters of 0.05 V/m (~7 μW/m^2). On average power density was 31 μW/m^2 and the 99th percentile amounted to 307 μW/m^2. A dichotomization at the 90th percentile (exposure above 0.1 V/m, corresponding to 26.5 μW/m^2) did not indicate any effect of exposure on the different outcome variables but effects of attribution on sleep quality and overall symptom score (v. Zerssen list).

This large study has a number of important advantages: it started from a representative sample of the German population with over 30,000 participants and the second phase with a regional subsample had a participation rate of 85%. Furthermore, several well-selected standardized tests were used in the second phase. Results of the first phase are essentially in line with the Austrian study of Hutter et al. [9]. Not only the fraction with attribution of health complaints to exposure from the base station (10%) is identical, but also the higher symptom score in proximity to the base station independent of concerns/attributions found in the previous study has been replicated. However, the study has also severe shortcomings, most notably: the failure to include a sufficient number of participants that can be considered as exposed to microwaves from the base station. Note that Hutter et al. [9] selected households based on the characteristics of the antennas in such a way as to guarantee a large exposure gradient. In the randomly selected households of the study by Blettner et al. [7] the 90th percentile used as cutoff was well below the median (~100 μW/m^2) of the earlier investigation and the 99th percentile was still below the level (500 μW/m^2) that was found to increase the prevalence of several symptoms. Therefore it is unlikely that the investigation of the second phase could detect an effect if it occurs at levels consistent with those reported by Hutter et al. [9].

2.2. Cancer

Despite considerable public concerns that exposure to microwaves from mobile phone base stations could be detrimental to health and may, in particular, cause cancer, up to now only two studies of cancer in the vicinity of base stations applying basically an ecological design have been published.

In a Bavarian town, Neila, the physicians of the town conducted an epidemiological investigation [14] to assess a possible association between exposure to base station radiation and cancer incidence. The design used was an improved ecological one. Two study areas were defined: one within a circle of 400 m radius around the only base stations (two that were located in close proximity to each other) of the town, and one area further than 400 m from the base stations. Within these defined areas streets were randomly selected (after exclusion of a street where a home for retired people was situated) and all general practitioners of the town that were active during the whole period of operation of the base stations (one base station started operation September 1993 the other December 1997) scanned their files for patients living in the selected streets. Overall 967 individuals were found, constituting approximately 90% of the reference population. The study period 1/1994 to 3/2004 was subdivided into two segments: The first 5 years of operation of the base station (1994 through 1998) and the period from the sixth year, 1999, until 3/2004. Among the identified individuals 34 incident cases of cancer (excluding non-melanoma skin cancer) were found. Assessment of cancer cases was assumed to be complete and all cases were verified histologically and by hospital discharge letters (note that there is no cancer registry in Bavaria). Age distribution was similar in the two areas with a mean age of 40.2 years in both, the area within 400 m of the base station and the area further apart. Crude annual cancer incidence in the first 5 years after start of operation of the base station was 31.3×10^{-4} and 24.7×10^{-4} in the closer and farther area, respectively. In the second period these figures were 76.7×10^{-4} and 24.7×10^{-4}. The age and gender adjusted expected value of incident cancer cases in the study population based on data from Saarland, a German county with a cancer registry, is 49×10^{-4}. In the second period cancer incidence in the area within 400 m of the base station was significantly elevated, both, compared to the area further away as well as compared to the expected background incidence. The incidence in the region further apart was reduced but not significantly when compared to the expected value.

Although this so-called Neila-study applied an improved ecological design with a random selection of streets and inclusion of some information from selected individuals, it is still subject to potential bias because relevant individual risk factors could not be included in the analyses.

A similar though less rigorous study has been performed in Netanya, Israel. Wolf and Wolf [15] selected an area 350 m around a base station that came into operation 7/1996. The population within this area belongs to the outpatient clinic of one of the authors. The cohort within this area consisted of 622 people living in this area for at least 3 years at study onset, which was one year after start of operation of the base station and lasted for 1 year. Overall cancer incidence within the study area was compared to a nearby region, to the whole city of Netanya, and to national rates. In the second year after onset of operation 8 cancer cases were diagnosed in the study area. In the nearby area with a cohort size of 1222 individuals, 2 cases were observed. Comparison to the total population with an expected incidence of 31×10^{-4} indicates a pronounced increase in the study area with an incidence of 129×10^{-4}. Also against the whole town of Netanya an increased incidence was noted especially in women. In an

addendum authors noted that also in the subsequent year 8 new cases were detected in the study area while in the period 5 years before the erection of the base station 2 cases occurred annually. Spot measurements of high frequency fields were conducted in the homes of cancer cases and values between 3 and 5 mW/m^2 were obtained. Although these values are well below guideline levels, they are quite high compared to typical values measured in randomly selected homes [7].

Also in the case of the Netanya study lack of information on individual risk factors makes interpretation difficult. Furthermore, migration bias has not been assessed although only subjects were included that occupied the area for at least 3 years. The short latency after start of operation of the base station rules out an influence of exposure on induction period of the diseases. The substantial increase of incidence is also hardly explainable by a promotional effect.

3. Experimental studies

3.1. Experiments in human sensitive and non-sensitive individuals

There are persons who claim to suffer from immediate acute as well as chronic effects on exposure to EMF and in particular to those from mobile phones or their base stations. Often these persons are called EMF hypersensitive (EHS). The preferred term agreed upon at a WHO workshop [16] was Idiopathic Environmental Intolerance with attribution to EMF (IEI-EMF). Indeed, it would be a misunderstanding to confuse EHS with allergic reactions; rather these persons react with different unspecific symptoms such as headaches, dizziness, loss of energy, etc. Whether these persons have actually the ability to tell the difference between situations with and without exposure to EMFs is an open question. In a recent review Röösli [17] concluded that "...the large majority of individuals who claim to be able to detect low level RF-EMF are not able to do so under double-blind conditions. If such individuals exist, they represent a small minority and have not been identified yet." However, it is important to differentiate between EMF sensitivity and sensibility [18]. Independent of the question whether or not there are individuals that sense the presence of low levels of EMFs such as those measured in homes near mobile phone base stations, there could well be an effect of such exposures on wellbeing and performance even under short-term exposure conditions. In several experimental investigations this question has been addressed by exposure of persons with self-reported symptoms and also in persons without known adverse reaction to an assumed exposure.

The first of these investigations was carried out by the Netherlands Organization for Applied Scientific Research (TNO) and published as a research report [19]. Two groups of persons were included in the experiment. One group consisted of individuals (25 females, 11 males) who have previously reported complaints and attributed them to GSM exposure. The other group consisted of subjects without such complaints (14 females, 22 males). Four experimental conditions were applied in a double-blind fashion: Sham exposure, exposure to 945 MHz GSM, 1840 MHz GSM, and 2140 MHz UMTS. Each participant underwent sham exposure and two of the active exposure conditions. Sequence of exposure was balanced such that each active exposure condition was tested equally often at each of three experimental sessions. Each experimental session and a training session lasted for 45 min. All three experimental sessions and the training session were completed on one day for each participant. Both, for GSM and UMTS exposure, a base station antenna was used and a simulated base station signal was transmitted during sessions. For the GSM conditions a 50% duty cycle (4 slots occupied) was applied with pulses of peak amplitudes of 1 V/m (0.71 V/m effective field strength; corresponding to 1.3 mW/m^2). For UMTS exposure a protocol was used with different low frequency components and an effective field strength of 1 V/m (corresponding to 2.7 mW/m^2). During each session several performance tests were conducted and immediately after each session a wellbeing questionnaire was administered (an adapted version of the Quality-of-Life Questionnaire of Bulpitt and Fletcher [20] with 23 items).

Overall score of wellbeing was significantly reduced in both groups after the UMTS condition compared to sham exposure. Considering subscores anxiety symptoms, somatic symptoms, inadequacy symptoms, and hostility symptoms were increased in the groups of sensitive individuals whereas in the control group only inadequacy symptoms were increased after UMTS exposure compared to sham. No effects were found in the two GSM exposure conditions. Concerning cognitive performance both groups revealed significant exposure effects in almost all tests in different exposure conditions. In most of these tests reaction time was reduced except for one simple reaction time task.

This study had an enormous echo both in the media as well as in the scientific community because it was the first experimental investigation with very low exposure to base station like signals and in particular to UMTS signals, and because it was conducted by a highly respected research institution reporting systematic effects of exposure that seemed to support citizens initiatives claiming that base stations have adverse effects on wellbeing and health. Immediately doubts were expressed that results could be biased due to a faulty methodology. In fact, study design can be improved. First of all testing all exposure conditions on the same day has the advantage to reduce variance from between day differences but could cause transfer effects if biological reactions do not immediately terminate after end of exposure and start of the next condition. Also time-of-day effect from chronobiological variations could be superimposing the reactions from exposure. Such effects are sometimes not removed by balancing exposure conditions. Second, not all subjects were tested under all exposure conditions. The decision to reduce total experimental duration by presenting only two of the three exposure conditions together with sham was sound but

on the other hand led to a reduced power. Several other arguments such as the different gender distribution in the two groups are not very important because each subject served as his/her own control and comparison between groups was not important in this investigation. Other criticism was expressed against statistical analysis. No correction for multiple testing was applied. While some advice protection against inflation of type I error others recommend correction only for crucial experiments and not for pilot studies like this. Another, more serious, criticism was put forward against disregarding sequence of experimental conditions. As mentioned above, sequence, transfer, and time-of-day effects could have compromised results because such effects are not completely removed by balancing exposure sequence. Due to this criticism several studies were planned that should investigate whether the effects observed in the TNO study are robust and could be replicated under improved study designs.

One of these experiments was performed in Switzerland [21]. Like in the TNO study, two groups of individuals were included: one with self-reported sensitivity to RF-EMF (radio-frequency EMF) and a reference group without complaints. The first group consisted of 33 persons (19 females, 14 males) and the reference group of 84 persons (43 females, 41 males). The experiment consisted of three experimental and one training session each 1 week apart performed on the same time of day (±2 h). Design was a randomized double-blind cross-over design like in the case of the TNO study, however, with a week between sessions and with all subjects tested under all experimental conditions that were solely simulated UMTS base station exposure at 1 V/m, 10 V/m and sham. The same UMTS protocol as in the TNO study was used. Each exposure condition lasted for 45 min. During exposure two series of cognitive tasks were performed. After each exposure condition the same questionnaire as has been used in the TNO study was applied and questions about sleep in the previous night, alcohol, coffee consumption, etc., were asked. Moreover, subjects had to rate the perceived field strength of the previous exposure condition on a visual analogue scale. In addition, before and after each session the short Questionnaire on Current Disposition [22] was answered by participants. Questionnaires were presented in a separate office room.

Except for a significant reduction of performance speed of sensitive participants in the 1 V/m condition in one of six cognitive tests no effect of exposure was detected. In particular, no reduction of wellbeing neither as assessed by the TNO questionnaire nor from scores of the Questionnaire on Current Disposition was found. Also correlation between perceived and real exposure was not more often positive than expected from chance. Fig. 2 compares results of the TNO study and the results of Regel et al. [21] for the matching conditions (UMTS at 1 V/m). There are some notable differences between the two studies: first, the reference group in the study of Regel et al. [21] had significantly higher scores (reduced wellbeing) as the reference group in the TNO study in both the sham and the UMTS 1 V/m condition; second,

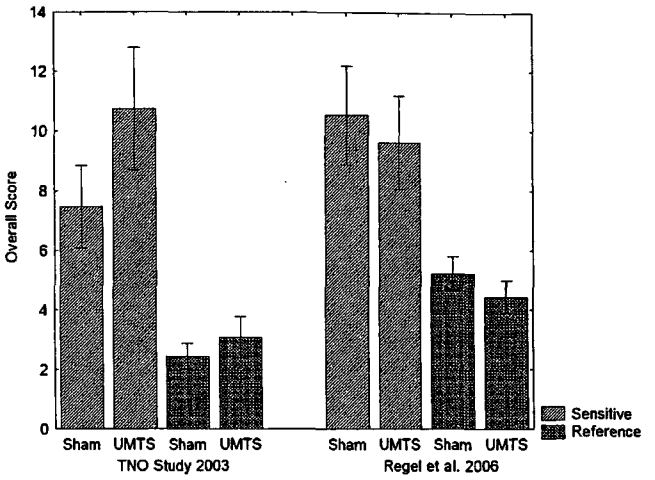


Fig. 2. Comparison of mean (±SEM) overall wellbeing scores (TNO questionnaire) obtained in the TNO study [19] and in the study of Regel et al. [21] for the matching conditions: Sham exposure and UMTS exposure at 1 V/m in sensitive participants and the reference group.

average scores from sensitive participants after exposure at 1 V/m are comparable in both studies but the sham condition resulted in much lower scores (better wellbeing) in the TNO study. There are several explanations for this difference between the two studies. It is possible that the reference group in the TNO study consisted of exceptionally robust individuals. The fraction of males was higher in the TNO study and males have typically lower scores. However, considering that the reference group in the TNO study was almost 10 years older (mean age 47 years) as compared to the study of Regel et al. [21] (mean age 38 years) this is not a satisfactory explanation. It is possible that the basic adversity of the experimental setup was higher in the latter study resulting in overall greater reduction of wellbeing. That this has not been observed in the sensitive group assumed to be more vulnerable to a 'nocebo' effect (the nocebo effect is the inverse of the placebo effect describing a situation when symptoms occur due to expecting adverse reactions) in both conditions could be due to a ceiling phenomenon. Although the study by Regel et al. [21] had an improved design and could not replicate the earlier findings of the TNO study, doubts exist whether this can be considered a refutation of an effect of UMTS exposure on wellbeing.

Another experimental study in sensitive and non-sensitive participants has been conducted in Essex, Great Britain, by Eltiti et al. [23]. The experiment consisted of two phases: an open provocation test and a series of double-blind tests. In the open provocation phase 56 self-reported sensitive and 120 non-sensitive control individuals participated. Of these, 44 sensitive (19 females, 25 males) and 115 controls (49 females, 66 males) also completed the double-blind tests. Participants took part in four separate sessions each at least 1 week apart. First session was the open provocation trial, sessions 2–4 were double-blind exposure trials with a sham, a GSM and a UMTS exposure condition. Double-blind sessions were reported to last for 1.5 h, however, Table 1 of the

article showed an overall length of 48 min only. GSM exposure was a simulated base station signal with both a 900 and a 1800 MHz component each at an average level of 5 mW/m^2 and with a simulated BCCH with all time slots occupied and a TCH with a simulated 40% call activity resulting in a total of 10 mW/m^2 GSM exposure at the position of the participants (corresponding to 1.9 V/m E-field strength). The UMTS signal had a frequency of 2020 MHz with a power flux density of 10 mW/m^2 over the area where the participant was seated. Traffic modeling for the UMTS signal was achieved using a test model representing a realistic traffic scenario, with high peak to average power changes. During double-blind sessions participants watched a BBC "Blue Planet" video for 20 min, performed a mental arithmetic task for 20 min, performed a series of cognitive tasks lasting 8 min, and made 'on/off' judgments. During the first 40 min every 5 min subjective wellbeing was recorded on visual analogue scales (VAS) measuring anxiety, tension, arousal, relaxation, discomfort, and fatigue. In addition a symptom scale consisting of 57 items was answered. During the whole period physiological measurements of heart rate, blood volume pulse, and skin conductance were performed.

Physiological measurements revealed higher average values for sensitive individuals compared to controls which were especially high under UMTS exposure conditions. Symptom list did not reveal any differences between double-blind conditions, but the overall frequency of solicited symptoms was low. Concerning subjective wellbeing as assessed by VAS there were increased values for anxiety, tension, and arousal under GSM and especially UMTS exposure conditions. Combining all scores of the six scales (with relaxation reflected) reveals a significant increase during UMTS exposure compared to sham for the sensitive group and a significant reduction for the control group (see Fig. 3). Judgment of participants about presence of exposure was not correct more often than inferred from chance.

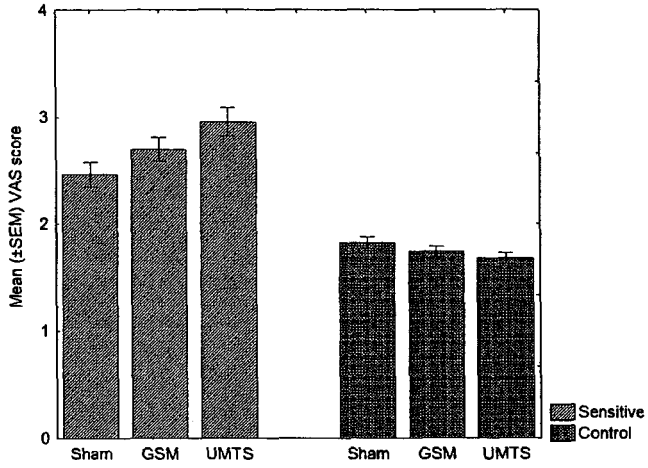


Fig. 3. Mean (±SEM) total visual analogue scale scores computed from Table 2 of Eltiti et al. [23] during sham, GSM, or UMTS exposure in sensitive and control individuals.

The increased values for anxiety, tension, and arousal found in this investigation were interpreted by the authors as due to an imbalance in the sequence of conditions with UMTS being more often the first exposure condition presented in the double-blind sessions. The imbalance was due to not reaching the predefined sample size. This points to the importance of setting the block size for randomization to a low level (e.g. in this experiment with 6 possible exposure sequences a block size of 18 would have been appropriate). Interpretation of authors, however, is questionable as pointed out by Röösli and Huss [24]. For arousal tabulated values stratified for sequence of presentation (Table 3 in [23]) demonstrates that the difference between sham and UMTS is present regardless of sequence of presentation. An additional analysis of the authors presented in response to the criticism in their statistical analysis seems to support their view that the observed difference to sham is due to a sequence effect. However, it seems that this analysis has not been correctly applied as the sequence was introduced as a between subjects factor which corrects only the interaction between group and condition. Also the figure they provided [23] is inconclusive as it only demonstrates what is already known: that first exposure leads to higher reduction of wellbeing (higher values of arousal). This investigation, although well designed and applying a more realistic exposure scenario than the other two studies, leaves some questions open. Despite an apparent corroboration of the findings of the TNO study, the imbalance in the sequence of exposures makes it difficult to decide whether the interpretation of authors that the observed effect is due to an excess number of UMTS exposures presented first in the sequence is correct or an actual effect occurred. Irrespective of these difficulties, consistent with the other investigations, wellbeing was not strongly affected.

There are several other investigations of a similar type that have been completed and already reported at scientific meetings (e.g. Watanabe, Japan; Augner, Austria, personal communication) but have not yet been published.

3.2. *Animal and in vitro experiments*

Anane et al. [25] applied the DMBA (7,12-dimethylbenz(a)anthracene) model of mammary tumor induction in female Sprague–Dawley rats to test whether a sub-chronic exposure to microwaves from a GSM-900 base station antenna affects tumor promotion or progression. Exposure was 2 h/day, 5 days/week for 9 weeks starting 10 days after application of 10 mg DMBA administered at an age of animals of 55 days. Exposure was applied in an anechoic chamber with animals placed in Plexiglas compartments that confined animals to a position parallel to the E-field. Details of the exposure protocol were not provided. Two series of experiments were conducted with four groups of 16 animals each. In the first experiment groups were: sham, 1.4, 2.2, and 3.5 W/kg whole-body SAR, and the second experiment with sham, 0.1, 0.7, and 1.4 W/kg. In the first experiment the tumor incidence rate was significantly increased at 1.4

and 2.2 W/kg exposure, while in the second experiment the incidence at 1.4 W/kg was significantly reduced.

The experiment by Anane et al. [25] is inconclusive not only because of the divergent results of the two experiments at the same exposure condition (1.4 W/kg SAR) but mainly because of the insufficient size of experimental groups. With a 70% background tumor incidence as observed in this investigation even for an increase to 100% in the exposed group the power to detect this difference at a significance level of 5% is less than 60%. Furthermore, considering experimental and biological variation substantial differences may occur by chance simply due to different distribution of background risk between experimental groups. Therefore, in contrast to the statement of authors that relevant differences would be detected with 16 animals per group, the study was severely underpowered and prone to spurious effects from uneven distribution of background risk. Also stress from confinement of animals could have contributed to the ambiguous results.

Yurekli et al. [26] report an experiment in male Wistar albino rats with the aim to analyze oxidative stress from whole-body exposure to a GSM 945 MHz signal at a SAR level of 11.3 mW/kg. In a gigahertz transverse (GTEM) cell a base station exposure in the far field was simulated. Two groups of rats, 9 animals in each group, were either exposed 7 h a day for 8 days or sham exposed. At the end of the exposure blood was withdrawn and malondialdehyde (MDA), reduced glutathione (GSH), and superoxide dismutase (SOD) were measured. MDA as well as SOD was significantly increased after exposure compared to sham, while GSH was significantly reduced. These results indicate that exposure may enhance lipid peroxidation and reduce the concentration of GSH which would increase oxidative stress. A disadvantage in this experiment was that the experiments were carried out sequentially and therefore animals differed in weight and no blinding could be applied.

In a series of experiments conducted in the Kashima Laboratory, Kamisu, Japan, different in vitro assays were applied to test whether irradiation with 2.1425 GHz, which corresponds to the middle frequency allocated to the down-link signal of IMT-2000 (International Mobile Telecommunication 2000, a 3G wide-band CDMA system), leads to cellular responses relevant for human health [27–29]. In the first experiment phosphorylation and gene expression of p53 was assessed [27]. In the second experiment heat-shock protein expression was evaluated in the human glioblastoma cell line A172 and human IMR-90 fibroblasts [28]. The effect of exposure of BALB/T3T cells on malignant transformation, on promotion in MCA (3-methylcholanthrene) treated cells, and on co-promotion in cells pretreated with MCA and co-exposed to TPA (12-O-tetradecanoylphorbol-13-acetate) was investigated by Hirose et al. [29]. In none of these experiments applying the same exposure regimen but different intensities and exposure durations (80 mW/kg SAR up to 800 mW/kg SAR, 2 h to several weeks) an effect of exposure was observed. Exposure facility comprised of two anechoic chambers allowing blinded simultaneous exposure of an array of 7 × 7 dishes in each chamber. Dishes were placed in a culture cabinet located in the anechoic chamber and exposed to radiation from a horn antenna whose signals were focused by a dielectric lens to obtain homogenous irradiation of the dishes. Details of the exposure protocol were not disclosed. It is stated that an IMT-2000 signal at a chiprate (a chip is a byte of information) of 3.84 Mcps was used for exposure. Assuming that it did not contain any low-frequency components as typically present in actual exposures the implications of the findings are unclear. It is rarely supposed that the high-frequency components of RF-EMFs itself are able to elicit any relevant effects in the 'low-dose' range. Rather low-frequency modulation may contribute to biological responses. Therefore, results of these Japanese investigations are of limited value for risk assessment, conditional on them having no such biologically relevant exposure attributes.

4. Discussion

Although there is considerable public concern about adverse health effects from long-term exposure to microwaves from mobile phone base stations there are only few studies addressing this issue. Several reasons can be identified for the scarcity of scientific investigations. First of all, WHO has discouraged studies of base stations, at least concerning cancer as endpoint, because retrospective assessment of exposure was considered difficult. Also COST 281 did not recommend studies of base stations and stated in 2002: "If there is a health risk from mobile telecommunication systems it should first be seen in epidemiological studies of handset use."

It is not appreciated that there are substantial and important differences between exposure to handsets and base stations. The typically very low exposure to microwaves from base stations, rarely exceeding 1 mW/m^2, was deemed very unlikely to produce any adverse effect. Assuming energy equivalence of effects a 24 h exposure at 1 mW/m^2 from a base station would be roughly equivalent to 30 min exposure to a mobile phone operating at a power of 20 mW (average output power in areas of good coverage). Because we do not know whether time-dose reciprocity holds for RF-EMF and whether there is a threshold for biological effects, there is no a priori argument why such low exposures as measured in homes near base stations could not be of significance for wellbeing and health. As an example from a different field of environmental health consider noise exposure: it is well known that at noise levels exceeding 85 dB(A) a temporary shift of hearing threshold occurs and that, besides this short-term effect, after years of exposure noise induced hearing loss may occur. On the other hand, at a sound pressure of more than a factor of 1000 below, when exposure occurs during the night, exposed individuals will experience sleep disturbances that could affect health in the long run. From this example it follows that exposure may have qualitatively different effects at different exposure levels.

The most important difference between mobile phone use and exposure from base station signals is duration of exposure. While mobile phones are used intermittently with exposure duration seldom exceeding 1 h per day, exposure to base stations is continuous and for up to 24 h a day. It has also to be mentioned that the exposure of mobile phone users is in the near field and localized at the head region, while base stations expose the whole body to the far field. Strictly speaking exposure from mobile phones and their base stations have almost nothing in common except for the almost equal carrier frequency that is likely of no importance for biological effects.

Concerning reconstruction of exposure to base station signals there is no greater difficulty than for retrospective assessment of exposure to mobile phones. It is not always necessary to determine exposure precisely. For epidemiological investigations it often suffices to have a certain gradient of exposures. As long as any two persons can be differentiated along such a gradient epidemiological investigations can and should be carried out.

There are seven field studies of wellbeing and exposure to base station signals available to date. Two were in occupational groups working in a building below [11] or below as well as opposite a building with a roof-mounted base station antenna [10]. The other five were in neighbors of base stations: Santini et al. [5,6], Navarro et al. [8], Hutter et al. [9], Blettner et al. [7], and Thomas et al. [12]. Studies had different methodologies with the least potential for bias in the studies of Hutter et al. [9] and Blettner et al. [7]. All other studies could be biased due to self-selection of study participants. One study explored personal dosimetry during 24 h [12] but results were inconclusive due to insufficient power and omission of nighttime measurements. The study of Blettner et al. [7] had an interesting design with a first phase in a large population based representative sample and a second phase with individual measurements in the bedrooms of participants that were a subgroup of the larger sample. Unfortunately this second sample did not contain a sufficiently large fraction of individuals with relevant exposure (99% had bedside measurements below 0.3 mW/m^2).

Despite some methodological limitations of the different studies there are still strong indications that long-term exposure near base stations affects wellbeing. Symptoms most often associated with exposure were headaches, concentration difficulties, restlessness, and tremor. Sleeping problems were also related to distance from base station or power density, but it is possible that these results are confounded by concerns about adverse effects of the base station, or more generally, by specific personality traits. While the data are insufficient to delineate a threshold for adverse effects the lack of observed effects at fractions of a mW/m^2 power density suggests that, at least with respect to wellbeing, around 0.5–1 mW/m^2 must be exceeded in order to observe an effect. This figure is also compatible with experimental studies of wellbeing that found effects at 2.7 and 10 mW/m^2.

There are regular media reports of an unusually high incidence of cancer in the vicinity of mobile phone base stations. Because there are several hundred thousand base stations operating all over the world some must coincide by chance with a high local cancer incidence. Regionally cancer incidence has a distribution with an overdispersion compared to the Poisson distribution. Overdispersion is predominantly due to variations in the distribution of age and gender. Therefore, a much higher number of cases than expected from average incidences can occur by chance. Unfortunately there are no multi-regional systematic investigations of cancer incidence related to mobile phone base stations available to date. Only studies in a single community, one in Bavaria [14] and one in Israel [15], have been published that reported a significantly increased incidence in an area of 400 and 350 m around a base station, respectively. Although incidence in proximity to the base station strongly exceeded the expected values and was significant even considering overdispersion in the case of the Neila study in Bavaria, still no far reaching conclusions can be drawn due to the ecological nature of the studies. However, both studies underline the urgent need to investigate this problem with an appropriate design. Neubauer et al. [30] have recommended focusing initially on short-term effects and 'soft' outcomes given the problems of exposure assessment. However, as has been mentioned previously, the problems of exposure assessment are less profound as often assumed. A similar approach as chosen in the study of leukemia around nuclear power plants [31] could be applied also for studying cancer in relation to base station exposure. Such a case–control design within areas around a sufficiently large sample of base stations would provide answers to the questions raised by the studies of Eger et al. [14] and Wolf and Wolf [15].

In 2003 the so-called TNO study [19] had received wide publicity because it was the first experimental investigation of short-term base station exposure in individuals that rated themselves sensitive to such signals. A lot of unfounded criticism was immediately raised such as complaints about the limited sample size and the not completely balanced design. But also valid arguments have been put forward. The consecutive tests with all experimental conditions presented one after the other could result in sequential effects that may not be completely removed by balancing the sequence of exposures. In several countries follow-up studies were initiated two of which have already been published [21,23]. One of these experiments partly supported the TNO study the other found no effect. While the study of Regel et al. [21] closely followed the conditions of the previous experiment only avoiding the shortcomings of a sequential within-day design and improvements by including two intensities of UMTS exposure, the study of Eltiti et al. [23] had a different procedure and included physiological measurements. Regel et al. [21] applied the same questionnaire as has been used in the TNO study. Because non-sensitive participants and sensitive participants during sham exposure (despite their almost 10 years younger age) reported considerably lower wellbeing,

it is possible that the experimental setup was more adverse and imposed too much stress such that these conditions confounded the effect of the base station exposure. Results of the other replication experiment of Eltiti et al. [23] may be compromised by an imbalance in the sequence of experiments with more sensitive participants receiving UMTS exposure in the first session. Hence, based on available evidence, it cannot be firmly decided whether such weak signals as applied in these experiments to simulate short-term base station exposure affects wellbeing.

Concerning animal experiments and in vitro investigations the data base is insufficient to date. While in vivo exposure of Wistar albino rats [26] imply an induction of oxidative stress or an interaction with antioxidant cellular activity, in vitro experiments [27] found no indication of cellular stress in human glioblastoma cells and fibroblasts. While some may be inclined to attribute effects in the low-dose range to experimental errors there is the possibility that the characteristics of the exposure that are relevant for an effect to occur simply vary in the experiments and lead to ambiguous results. As long as these decisive features of the exposure (if they actually exist) are unknown and in particular the type and components of low-frequency modulation vary across experiments, it is impossible to coherently evaluate the evidence and to come to a science based conclusion.

Overall results of investigations into the effects of exposure to base station signals are mirroring the broader spectrum of studies on handsets and on RF-EMF in general. There are indications from epidemiology that such exposures affect wellbeing and health weakly supported by human provocation studies and an inconclusive body of evidence from animal and in vitro studies.

References

[1] N. Leitgeb, J. Schröttner, M. Böhm, Does "electromagnetic pollution" cause illness? An inquiry among Austrian general practitioners, Wien. Med. Wochenschr. 155 (9–10) (2005) 237–241.

[2] A. Huss, M. Röösli, Consultations in primary care for symptoms attributed to electromagnetic fields—a survey among general practitioners, BMC Public Health 30 (6) (2006) 267.

[3] M. Kundi, F. Schinner, W. Mosgöller, H.-P. Hutter, Proceedings of the International Workshop on Possible Biological and Health Effects of RF Electromagnetic Fields, 25–28 October, University of Vienna, 1998.

[4] WHO 2006, WHO Research Agenda for Radio Frequency Fields.

[5] R. Santini, P. Santini, J.M. Danze, P. Le Ruz, M. Seigne, Enquête sur la santé de riverains de stations relais de téléphonie mobile: I/Incidences de la distance et du sexe, Pathol. Biol. (Paris) 50 (2002) 369–373.

[6] R. Santini, P. Santini, J.M. Danze, P. Le Ruz, M. Seigne, Enquête sur la santé de riverains de stations relais de téléphonie mobile: II/Incidences de l'âge des sujets, de la durée de leur exposition et de leur position par rapport aux antennes et autres sources électromagnétiques, Pathol. Biol. (Paris) 51 (2003) 412–415.

[7] M. Blettner, B. Schlehofer, J. Breckenkamp, B. Kowall, S. Schmiedel, U. Reis, P. Potthoff, J. Schüz, G. Berg-Beckhoff, Querschnittstudie zur Erfassung und Bewertung möglicher gesundheitlicher Beeinträchtigungen durch die Felder von Mobilfunkbasisstationen, BfS (2007).

[8] E.A. Navarro, J. Segura, M. Portoles, C. Gomez-Perretta de Mateo, The microwave syndrome: a preliminary study in Spain, Electromag. Biol. Med. 22 (2003) 161–169.

[9] H.-P. Hutter, H. Moshammer, P. Wallner, M. Kundi, Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations, Occup. Environ. Med. 63 (2006) 307–313.

[10] G. Abdel-Rassoul, O. Abou El-Fatech, M. Abou Salem, A. Michael, F. Farahat, M. El-Batanouny, E. Salem, Neurobehavioral effects among inhabitants around mobile phone base stations, Neurotoxicology 28 (2) (2006) 434–440.

[11] S. Heinrich, A. Ossig, S. Schlittmeier, J. Hellbrück, Elektromagnetische Felder einer UMTS-Mobilfunkbasisstation und mögliche Auswirkungen auf die Befindlichkeit—eine experimentelle Felduntersuchung, Umwelt. Med. Forsch. Prax. 12 (2007) 171–180.

[12] S. Thomas, A. Kühnlein, S. Heinrich, G. Praml, D. Nowak, R. von Kries, K. Radon, Personal exposure to mobile phone frequencies and well-being in adults: a cross-sectional study based on dosimetry, Bioelectromagnetics 29 (2008) 463–470.

[13] K. Radon, H. Spegel, N. Meyer, J. Klein, J. Brix, A. Wiedenhofer, H. Eder, G. Praml, A. Schulze, V. Ehrenstein, R. von Kries, D. Nowak, Personal dosimetry of exposure to mobile telephone base stations? An epidemiologic feasibility study comparing the Maschek dosimeter prototype and the Antennessa SP-090 system, Bioelectromagnetics 27 (2006) 77–81.

[14] H. Eger, K.U. Hagen, B. Lucas, P. Vogel, H. Voit, Einfluss der räumlichen Nähe von Mobilfunksendeanlagen auf die Krebsinzidenz, Umwelt-Medizin-Gesellschaft 17 (2004) 273–356.

[15] R. Wolf, D. Wolf, Increased incidence of cancer near a cellphone transmitter station, Int. J. Cancer Prev. 1 (2004) 123–128.

[16] K. Hansson Mild, M. Repacholi, E. van Deventer, P. Ravazzani (Eds.), 2006. Working Group Report. In: Proceedings International Workshop on EMF hypersensitivity, 25–27 October 2004, Prague, Czech Republic. Milan: WHO Press, pp. 15–26. Available from: http://www.who.int/peh-emf/publications/reports/EHS_Proceedings_June2006.pdf, accessed August 2008.

[17] M. Röösli, Radiofrequency electromagnetic field exposure and non-specific symptoms of ill health: a systematic review, Environ. Res. 107 (2008) 277–287.

[18] N. Leitgeb, J. Schröttner, Electrosensibility and electromagnetic hypersensitivity, Bioelectromagnetics 24 (2003) 387–394.

[19] A.P.M. Zwamborn, S.H.J.A. Vossen, B.J.A.M. van Leersum, M.A. Ouwens, W.N. Mäkel, Effects of Global Communication System Radio-Frequency Fields on Well being and Cognitive Functions of Human Subjects with and without Subjective Complaints. FEL-03-C148, TNO, The Hague, the Netherlands, 2003.

[20] C.J. Bulpitt, A.E. Fletcher, The measurement of quality of life in hypertensive patients: a practical approach, Br. J. Clin. Pharmacol. 30 (1990) (1990) 353–364.

[21] S.J. Regel, S. Negovetic, M. Röösli, V. Berdinas, J. Schuderer, A. Huss, U. Lott, N. Kuster, P. Achermann, UMTS base station like exposure, well being and cognitive performance, Environ. Health Perspect. 114 (2006) 1270–1275.

[22] B. Müller, H.D. Basler, Kurzfragebogen zur Aktuellen Beanspruchung (KAB), Beltz, Weinheim, Germany, 1993.

[23] S. Eltiti, D. Wallace, A. Ridgewell, K. Zougkou, R. Russo, F. Sepulvelda, D. Mirshekar-Syahkal, P. Rasor, R. Deeble, E. Fox, Does short-term exposure to mobile phone base station signals increase symptoms in individuals who report sensitivity to electromagnetic fields? A double-blind randomised provocation study, Environ. Health Perspect. 115 (2007) 1603–1608.

[24] M. Röösli, A. Huss, Mobile phone base station exposure and symptoms, Environ. Health Perspect. 116 (2008) A62–A63.

[25] R. Anane, P.E. Dulou, M. Taxile, M. Geffard, F.L. Crespeau, B. Veyret, Effects of GSM-900 microwaves on DMBA-induced mammary gland tumors in female Sprague–Dawley rats, Radiat. Res. 160 (2003) 492–497.

[26] A.I. Yurekli, M. Ozkan, T. Kalkan, H. Saybasili, H. Tuncel, P. Atukeren, K. Pinar, K. Gumustas, S. Seker, GSM base station electromagnetic radiation and oxidative stress in rats, Electromag. Biol. Med. 25 (2006) 177–188.

[27] H. Hirose, N. Sakuma, N. Kaji, T. Suhara, M. Sekijima, T. Nojima, J. Miyakoshi, Phosphorylation and gene expression of p53 are not affected in human cells exposed to 2.1425 GHz band CW or W-CDMA modulated radiation allocated to mobile radio base stations, Bioelectromagnetics 27 (2006) 494–504.

[28] H. Hirose, N. Sakuma, N. Kaji, K. Nakayama, K. Inoue, M. Sekijima, T. Nojima, J. Miyakoshi, Mobile phone base station emitted radiation does not induce phosphorylation of hsp27, Bioelectromagnetics 28 (2007) 99–108.

[29] H. Hirose, T. Suhara, N. Kaji, N. Sakuma, M. Sekijima, T. Nojima, J. Miyakoshi, Mobile phone base station radiation does not affect neoplastic transformation in BALB/3T3 cells, Bioelectromagnetics 29 (2008) 55–64.

[30] G. Neubauer, M. Feychting, Y. Hamnerius, L. Kheifets, N. Kuster, I. Ruiz, J. Schüz, R. Überbacher, J. Wiart, Feasibility of future epidemiological studies on possible health effects of mobile phone base stations, Bioelectromagnetics 28 (2007) 224–230.

[31] P. Kaatsch, C. Spix, R. Schulze-Rath, S. Schmiedel, M. Blettner, Leukaemia in young children living in the vicinity of German nuclear power plants, Int. J. Cancer 122 (2008) 721–726.

ELSEVIER

Pathophysiology 16 (2009) 137–147

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Review

Estimating the risk of brain tumors from cellphone use: Published case–control studies

L. Lloyd Morgan *

1324 Solano Ave. Apt. 11, Albany, CA 94706, United States

Received 21 November 2008; accepted 30 January 2009

Abstract

This paper reviews the results of early cellphone studies, where exposure duration was too short to expect tumorigenesis, as well as two sets of more recent studies with longer exposure duration: the Interphone studies and the Swedish studies led by Dr. Lennart Hardell. The recent studies reach very different conclusions. With four exceptions the industry-funded Interphone studies found no increased risk of brain tumors from cellphone use, while the Swedish studies, independent of industry funding, reported numerous findings of significant increased brain tumor risk from cellphone and cordless phone use. An analysis of the data from the Interphone studies suggests that either the use of a cellphone *protects* the user from a brain tumor, or the studies had serious design flaws. Eleven flaws are identified: (1) selection bias, (2) insufficient latency time, (3) definition of 'regular' cellphone user, (4) exclusion of young adults and children, (5) brain tumor risk from cellphones radiating higher power levels in rural areas were not investigated, (6) exposure to other transmitting sources are excluded, (7) exclusion of brain tumor types, (8) tumors outside the cellphone radiation plume are treated as exposed, (9) exclusion of brain tumor cases because of death or illness, (10) recall accuracy of cellphone use, and (11) funding bias. The Interphone studies have all 11 flaws, and the Swedish studies have 3 flaws (8, 9 and 10). The data from the Swedish studies are consistent with what would be expected if cellphone use were a risk for brain tumors, while the Interphone studies data are incredulous. If a risk does exist, the public health cost will be large. These are the circumstances where application of the Precautionary Principle is indicated, especially if low-cost options could reduce the absorbed cellphone radiation by several orders of magnitude.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Electromagnetic field; Cellphone; Brain tumor; Mobile phone; Cellular phone; Cordless phone; Glioma; Acoustic neuroma; Meningioma; Funding; Interphone

Contents

1. Introduction 138
2. Early case–control cellphone studies 138
3. The industry-funded Interphone study 138
   3.1. Flaw 1: selection bias 140
   3.2. Flaw 2: insufficient latency time 140
   3.3. Flaw 3: definition of "regular" cellphone user 141
   3.4. Flaw 4: exclusion of young adults and children 141
   3.5. Flaw 5: brain tumor risk from cellphones radiating higher power levels in rural areas were not investigated 141
   3.6. Flaw 6: exposure to other transmitting sources are not considered 141
   3.7. Flaw 7: exclusion of brain tumor types 141
   3.8. Flaw 8: tumors outside the cellphone's radiation plume are treated as exposed 142
   3.9. Flaw 9: exclusion of brain tumor cases because of death or too ill to respond 142

* Tel.: +1 510 528 5302.
E-mail address: bilovsky@aol.com.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.009

3.10. Flaw 10: recall accuracy of cellphone use 142
3.11. Flaw 11: funding bias 142
4. Increased risk Interphone laterality findings 143
5. The independently funded Swedish studies led by Dr. Lennart Hardell 144
6. Role of industry 144
6.1. Insufficient funding 144
7. Potential public health impact 145
8. Precautionary Principle 145
9. Conclusions 146
Conflicts of interest 146
References 146

1. Introduction

This review covers all case–control studies on the risk of brain tumors from cellphone use published up to March 2009 and does not include epidemiological studies on the risk of brain tumors from exposure to other sources of electromagnetic fields (EMFs). It examines the strengths and weaknesses of these studies and what can be learned from differences in the findings. Because certainty is not possible in science, much less in epidemiology, the indication of a possible risk of brain tumors from cellphone use suggests that the Precautionary Principle be applied.

In almost all epidemiological investigations of rare diseases, such as brain tumors, researchers use what is known as a case–control design. Cases are subjects who have the disease and controls are randomly chosen subjects without the disease. Typically controls are matched to the cases by age, gender, geographical area, and income. Subjects are asked a set of questions, which for a cellphone study would include questions about their cellphone use.

The Odds Ratio (OR), the increased risk (OR > 1.0), or decreased risk (OR < 1.0) of brain tumors as a result of exposure to cellphone radiation is reported. A two-by-two table is used to calculate the Odds Ratio. In Table 1, Case and Control subjects are in the rows and Exposed and Unexposed subjects are in the columns. The Odds Ratio = (Exposed Cases) × (Unexposed Controls)/(Exposed Controls) × (Unexposed Cases).

Actual studies use sophisticated statistical regression analysis to adjust for confounding effects (age, gender, smoking, etc.), but the basic concept is the same. Additionally, along with the Odds Ratio, a 95% confidence interval (CI) is reported.

In this discussion cellphone studies are grouped into early studies and later studies. The later studies are presented as two sets of studies. Since each set uses a common protocol, each can be considered a single study: The two sets are the industry-funded Interphone studies and the independently funded Swedish studies led by Dr. Lennart Hardell.

2. Early case–control cellphone studies

The salient fact of these early studies is the short duration of cellphone use. It would have been surprising to find any risk of a brain tumor, because an increased risk would have required a short latency time between exposure and diagnosis. Indeed, none of these studies reported finding a significant risk ($p \leq 0.05$) of a brain tumor from cellphone use. Yet, as can be seen in Table 2, each study did find a non-significant ($p > 0.05$) increased risk including two near-significant findings of increased risk ($p < 0.10$). And, Auvinen et al. found that for each year of cellphone use a significant 20% increased risk of a brain cancer (glioma). Table 2 summarizes these studies [1–5].

Perhaps these early studies that found no significant risk had actually found an early warning of trouble ahead.

3. The industry-funded Interphone study

The Interphone study is a 13-country case–control study on the risk of brain and salivary gland tumors from cellphone use. The Interphone study uses a standard protocol such that all individual country results can be pooled together to increase the power of the study. This discussion is limited to the brain tumors studies.

As of December 2008 there have been 11 single-country and 3 multi-country Interphone brain tumor studies published [6–19]. The multi-country studies will not be discussed

Table 1
Simple example of increased risk.

	Exposed	Unexposed	Totals
Cases	60	40	100
Controls	49	51	100
Totals	109	91	200
Odds Ratio	1.56		

Table 2
Early cellphone case–control studies.

Study	Cases	Eligibility		Av. use time years	Major findings				Comments
		Start	End		OR	95% CI		p value	
Hardell et al., May 2000 [1]	209	1994–1996 (Uppsala-Orebro) 1995–1996 (Stockholm)		Not reported	2.42	0.97	6.05	0.053†	Temporal, parietal, occipital lobes—ipsilateral use (number of cases not reported)
Muscat et al., December 2000[a] [2]	469	1994	1998	2.8	2.1	0.9	4.7	0.073†	Neuroepithelial cancer (35 cases)
Inskip et al., January 2001 [3]	782	June-94	August-98	Not reported	1.9	0.6	5.9	0.26	Acoustic neuroma, ≥5 years of use (5 cases)
Muscat et al., May 2002[a] [4]	90	1997	1999	4.1	1.7	0.5	5.1	0.36	Acoustic neuroma, 3–6 years of use (11 cases)
Auvinen et al., May 2002[a] [5]	398		1996	Av. 2–3 (analog) <1 (digital)	1.7	0.9	3.5	0.12	Glioma, >2 years of use (number of cases not reported)
					1.2	1.0	1.4	0.050	Glioma, increase risk per year (number of cases not reported)

Bold indicates statistically significant ($p \leq 0.05$).
[a] Industry funded study.
† Near-significant ($p \leq 0.10$).

Table 3
Summary data of the 11 Interphone studies investigated.

Study, Country	Tumor	Dx eligibility range years	% Cases ≥10 years	% of eligible controls refusing participation	"Regular" use from abstract	
					OR	CI
Lönn et al. 2004, Sweden	AN	3.0	9.5%	27.9%	1.0	0.6 to 1.5
Christensen et al. 2004, Denmark	AN	2.0	1.4%	36.0%	0.90	0.51 to 1.57
Lönn et al. 2005, Sweden	G	2.0	6.7%	29.5%	**0.8**	0.6 to 1.0
	M		4.4%		**0.7**	0.5 to 0.9
Christensen et al. 2005, Denmark	L-g G	2.0	5.6%	36.0%	1.08	0.58 to 2.00
	H-g G				**0.58**	0.34 to 0.90
	M		3.4%		1.00	0.54 to 1.28
Schüz et al. 2006, Germany	G	3.0	3.3%	39.0%	0.98	0.74 to 1.29
	M		1.3%		0.84	0.62 to 1.13
Takebayashi et al. 2006, Japan	AN	3.9	8.2%	15.8%	0.73	0.43 to 1.23
Klaeboe et al. 2007, Norway	AN	2.0	0.0%	31.0%	**0.5**	0.2 to 1.0
	G		0.0%		**0.6**	0.4 to 0.9
	M		0.0%		0.8	0.5 to 1.1
Hours et al. 2007, France	AN	2.5	0.0%	28.8%	0.92	0.53 to 1.59
	G		0.0%		1.15	0.65 to 2.05
	M		0.0%		0.74	0.43 to 1.28
Hepworth et al., 2007, United Kingdom	G	3.3	6.8%	65.5%	0.94	0.78 to 1.13
Schlehofer et al., 2007, Germany	AN	3.1	0.0%	45.1%	0.67	0.38 to 1.19
Takebayashi et al. 2008, Japan	G	3.9	2.3%	56.3%	1.22	0.63 to 1.27
	M		4.5%	12.9%	0.70	0.42 to 1.16
Weighted average (by cases)		**2.7**	**6.2%**	**40.7%**		
Wt. Av. (by cases) excluding Lönn (2004) and Hepworth		**2.7**	**6.2%**	**33.4%**		

AN = acoustic neuroma; G = glioma; M = meningioma; L-g G = low-grade glioma; H-g G = high-grade glioma. Bold OR indicates statistically significant protection.

further because they overlap the single-country studies [17–19]. Table 3 summarizes the 11 Interphone studies included in this analysis. Three studies had no cases who had used a cellphone for ≥10 years [12,14,16]. For Odds Ratios (ORs) on the risk of brain tumors from "regular" cellphone use (reported in the abstracts) there were 15 ORs <1.0—a protective result (4 with significant protection), and 2 ORs were >1.0—a result indicating increased risk. The cumulative binomial probability of having 15 ORs <1.0 and 2 ORs >1.0 is highly unlikely ($p = 0.0012$) and indicates a significant protective effect.

Table 3 summarizes the 11 Interphone studies analyzed in this paper. It shows the years available for case diagnosis (Dx) to be eligible for participation in the study, the percentage of cases that used a cellphone for 10 or more years, the percentage of selected controls that refused to participate in the study, and the Odds Ratios of brain tumors for "regular" cellphone use reported in the abstract of each paper. Finally, weighted (by cases) averages are presented for the Dx years for eligibility in the studies, the % of cases that used a cellphone for ≥10 years, and the % of eligible controls that refused participation.

All 14 of these Interphone brain tumor studies have found that use of a cellphone *protects* the user from a brain tumor. The 11 studies reported a total of 284 statistically independent ORs; 217 ORs <1.0 and 67 ORs >1.0 ($p = 6.2 \times 10^{-20}$). There are two possibilities to explain such an incredulous result: (1) Either use of a cellphone provides protection from a brain tumor, or (2) the Interphone Protocol [20] has serious design flaws.

Eleven design flaws have been identified. The consistent findings of protection can be explained because 8 of these 11 flaws underestimate the risk of brain tumors.

3.1. Flaw 1: selection bias

In a case–control cellphone study both cases and controls are asked if they would like to participate in the study. It is reasonable to assume controls who use a cellphone are more likely to participate than controls who do not use a cellphone. This would result in selection bias. And, such selection bias would result in an underestimation of risk.

The impact of selection bias increases as the percentage of controls that refuse to participate increases. The Interphone control weighted-average refusal rate was a remarkably high 41%. Dr. Sam Milham, an occupational epidemiologist with over 100 published papers, states that in the past, science journals would not accept a study with such a high refusal rate [21].

One Interphone study investigated the possibility of selection bias by asking controls that refused participation if they used a cellphone; 34% said they used a cellphone and 59% said they did not use a cellphone, confirming selection bias in that study [6].

How could selection bias have been mitigated? First, do not tell subjects the study is a cellphone study. Second, pay the subjects for participation in the study. The result would be a higher participation rate, and more importantly, control participation would not be biased for use, or non-use of a cellphone. However, given the funding provided, paying subjects was not considered.

Table 4
Odds Ratios, with and without selection bias.

	Exposed	Unexposed	Totals
With selection bias			
Cases	60	40	100
Controls	***60***	40	100
Totals	120	80	200
Odds Ratio	1.00		

	Truly Exposed	Unexposed	Totals
Without selection bias			
Cases	60	40	100
Controls	***49***	51	100
Totals	109	91	200
Odds Ratio	1.54		

Exposed Controls = (60 user "participating" controls) × (59% participation) + (34 cellphone users among non-participating controls) × (41% non-participants) = 49.

Table 4, using semi-hypothetical data (i.e., data that approximates actual Interphone data), illustrates how the Odds Ratios will change when selection bias exists and when the selection bias has been eliminated. As can be seen the Odds Ratio increases from 1.00 (no risk) to 1.54. Inversely stated, with selection bias a finding of no risk would mask an actual risk.

3.2. Flaw 2: insufficient latency time

The known latency time (the time between exposure and diagnosis) for brain tumors is 30+ years [22], similar to lung cancer from smoking [23] and mesothelioma from asbestos exposure [24]. Ten or more years was the longest cellphone use time reported. The weighted-average of brain tumors cases with ≥10 years of cellphone use was 6.2% of all cases, or 16 cases per study. Not including sufficient numbers of longer-term cellphone users results in an underestimation of risk.

To resolve this problem would require about a 3-fold increase in subjects. Because the weighted-average diagnosis eligibility time was only 2.7 years (the date range for cases to be diagnosed with a brain tumor to be eligible for the study), only a small number of subjects were available. There was insufficient funding to increase the eligibility time.

It is worth noting, two independently funded cellphone case–control studies, used a 6-year eligibility time. These two studies showed a consistent risk of brain tumors for ≥10 years of cellphone use [25,26].

3.3. Flaw 3: definition of "regular" cellphone user

The Interphone Protocol defines "regular" cellphone use as use for at least once a week for 6 months or more with any cellphone use 1 year prior to diagnosis excluded. Based on UK cellphone subscriber data [27] and the UK study's Dx eligibility dates [13], the rapid rise of cellphone use finds 85% of "regular" UK users had used a cellphone for less than 5 years; 98% of "regular" UK users had used a cellphone for less than 10 years (all Interphone countries have similar rapid increases in cellphone users). Given known latency times how could any risk of brain tumors be expected for "regular" users? Inclusion of such a large proportion of short-term users underestimates the risk of brain tumors.

Dr. Elizabeth Cardis, the head of the Interphone study stated, "Reporting 'regular' user [data] was not intended to be a risk factor." [28]. Yet, the abstract of every Interphone brain tumor study highlights that there is no risk of brain tumors from "regular" cellphone use.

3.4. Flaw 4: exclusion of young adults and children

The Interphone Protocol requires subjects to be between 30 and 59 years of age (some studies have included ages as low as 20). There is strong evidence that the young adults and children are at greater risk from exposure to carcinogens than mature adults suggesting that the young, with greater cell growth, are more vulnerable to genetic mutations.

Two cellphone studies report higher brain tumor risks in young adults (20–29 years of age) compared to mature adults. The first study found a 7-fold increased risk of brain tumor compared to a 1.40-fold risk for all adults [29], and the second study found a 3.2-fold risk of brain tumor [30] compared to <2-fold risk in older adults. An ionizing radiation brain tumor study found the younger a child's age, the greater the risk of brain tumors (4.6-fold/Gy risk of brain tumors for children less than 5 years of age; 3.2-fold/Gy risk for children 5 to 9 years of age, and; 1.47-fold/Gy risk for children 10 or more years) [22].

Inclusion of additional cases below 30 years would have provided greater insight into risk, but the additional cases would have increased the cost of the study.

3.5. Flaw 5: brain tumor risk from cellphones radiating higher power levels in rural areas were not investigated

Because rural users are farther away from the cell towers compared to urban users, the cellphone's radiated power is higher [31]. Unfortunately the Interphone studies selected mostly metropolitan areas to locate brain tumor cases. When higher radiated power is not included there is an underestimation of risk.

In order to have sufficient cases to achieve statistical power, the total number of cases and controls who live in rural areas would have to be increased. This would require additional funding compared to what was provided.

Table 5
Change in Odds Ratios cordless phone use is not included and when it is included.

	Exposed	Unexposed	Totals
Cordless phone exposure treated as unexposed			
Cases	*43*	57	100
Controls	*27*	73	100
Totals	70	130	200
Odds Ratio	2.0		

	Truly exposed	Unexposed	Totals
Cordless phone exposure treated as exposed			
Cases	*64*	36	100
Controls	*40*	60	100
Totals	104	96	200
Odds Ratio	2.6		

Truly Exposed Controls = (27 "Exposed" Controls) × (64 truly exposed cases/43 "Exposed" Cases) = 40.

3.6. Flaw 6: exposure to other transmitting sources are not considered

Subjects who use cordless phones, walkie-talkies, Ham radio transmitters, etc. are treated as unexposed in the Interphone study when in fact they are exposed. Again, it is important to note that two independently funded cellphone case–control studies treated cordless phone use as exposed, and found that cordless phone use results in an increased risk of brain tumors [25,26]. Treating exposed subjects as unexposed, once again, underestimates the risk of brain tumors.

Table 5 illustrates how the Odds Ratio would change if cordless phone users had been treated as exposed subjects. The first Odds Ratio table assumes a 2.0-fold risk. Additionally it assumes that 57% of cases did not use a cellphone (without considering cordless phone use). The second table assumes when cordless phone use is considered that the number of unexposed cases decreases to 36%. An additional assumption is cordless phones have the same risk of brain tumors as do cellphones. Given these assumptions we see that the inclusion of cordless phone use as an exposure increased the 2.0-fold risk to a 2.6-fold risk.

3.7. Flaw 7: exclusion of brain tumor types

The Interphone study includes three brain tumor types: acoustic neuroma, glioma and meningioma. Other types are excluded (e.g. brain lymphoma, neuroepithelial, etc.). Exclusion of these other tumors underestimates the risk of brain tumors.

Interestingly, as shown in Table 2 above, another industry-funded study reported a 2.1-fold risk of a neuroepithelial brain tumor [2] and an industry-funded cellphone study showed an excess risk of lymphoma in mice [32]. Given this knowledge it is surprising that all brain tumor types were not included.

3.8. Flaw 8: tumors outside the cellphone's radiation plume are treated as exposed

The radiation plume's volume is a small proportion of the brain's volume. Treating tumors outside the radiation plume as exposed tumors results in an overestimation of risk (the only flaw that overestimates risk).

The adult brain absorbs the cellphone's radiation almost entirely on the side of the head where the cellphone is held (ipsilateral); almost no radiation is deposited on the opposite side of the head (contralateral). In adults the ipsilateral temporal lobe absorbs 50–60% of the total radiation and is ~15% of the brain's volume. The ipsilateral cerebellum absorbs 12–25% of the total radiation and is ~5% of the brain's volume. Thus, 62–85% of the cellphone's radiation is absorbed by ~20% of an adult's brain's volume [33]. Because a child's brain absorbs far more radiation than an adult's brain, this data are not applicable for a child's brain.

Table 6, using semi-hypothetical data, shows how the Odds Ratio will change when all tumors are treated as exposed and when only tumors within the cellphone's radiation plume are treated as exposed. This hypothetical example assumes there is a 2.0-fold risk when all tumors are treated as exposed, and assumes that only 20% of the tumors are actually exposed. Per these assumptions, the apparent 2.0-fold risk is reduced to a 1.6-fold risk.

Because the proportion of all brain tumors to the tumors within the radiation plume is small, a larger (roughly 5-fold) number of subjects would be required. However, the funding provided, did not allow for such a large increase in subjects.

A recent paper showing changes in the brain's blood brain barrier (BBB) permeability reported, counter-intuitively, that the effect of the highest permeability of the BBB (highest leakage) occurs at lower exposures [34]. The effect of this phenomenon is that almost all the leakage from a GSM cellphone occurs deep in the brain and on the contralateral side.

Table 6
Odds Ratios with all tumors exposed and without all tumors exposed.

	Exposed	Unexposed	Totals
With flaw 8 design error			
Cases	75	25	100
Controls	60	40	100
Totals	135	65	200
Odds Ratio	2.0		
	Truly exposed	**Unexposed**	**Totals**
Without flaw 8 design error			
Cases	**15**	70	85
Controls	**12**	88	100
Totals	27	158	185
Odds Ratio	1.6		

Truly Exposed Cases = (75 "exposed" cases) × (20% brain exposed) = 15.
Truly Exposed Controls = (60 "exposed" controls) × (20% brain exposed) = 12.

Whether this is similar for the induction of brain tumors is unknown. However, whether or not it is similar does not negate the fact that the cellphone's radiation plume is in a small proportion of the total brain's volume.

3.9. Flaw 9: exclusion of brain tumor cases because of death or too ill to respond

A large number of brain cancer (glioma) cases died before they could be interviewed or were too ill to be interviewed. Common practice would be to interview a proxy (e.g., a spouse). The Interphone Protocol requires use of proxies in case of death [20], yet 3 of the 7 glioma studies excluded deceased, or too ill to be interviewed cases from their studies [9,12,13] and a 4th did not use proxies for all of the cases who were too ill to be interviewed or who had died [10]. The weighted average of these exclusions was 23% of all glioma cases. This flaw limits determining the risks, if any, from the most deadly and debilitating brain tumors from cellphone use.

Another study found significant risks for high-grade glioma (the most deadly), but not for low-grade glioma (the least deadly) [35].

3.10. Flaw 10: recall accuracy of cellphone use

Memory accuracy, particular in the distant past, is limited at best. The Interphone project investigated this problem by asking cellphone users to recall their cellphone use, and then compared the recall to billing records.

The study reported that light cellphone users tend to underestimate their use and heavy users tend to overestimate their use. This results in an underestimation of risk [36].

Accurate data for the Interphone study could have been obtained by accessing subjects' cellphone-billing records as was done in the study of recall bias [36]. It is reasonable to assume that the available funding did not support the gathering of billing records.

3.11. Flaw 11: funding bias

If studies are funded by an entity with a financial interest in the findings, it has been shown that, more often than not, the findings of such a study are favorable to the financial interest compared to studies where the funding has no financial interest.

Dr. Henry Lai at Washington University in Seattle maintains a database of cellphone biological studies. The results (Table 7) from his database (July 2007) report the magnitude of funding bias. The industry-funded studies found an effect in 28% of the studies and the independently funded studies found an effect 67% of the time. The probability that this is a chance finding is extraordinarily minute ($p = 2.3 \times 10^{-9}$).

A study on the source of funding of cellphone studies and the reported results reported, "We found that the studies funded exclusively by industry were indeed substantially less likely to report statistically significant effects on a range of

Table 7
Industry-funded and independently funded cellphone biological studies.

		Cellphone biological studies					
		Effect found		No effect found		Studies	% all studies
		Studies	% all studies	Studies	% all studies		
Industry funded	No.	27	8.3%	69	21.2%	96	29.4%
	%	28.1%		71.9%			
Independently funded	No.	154	47.5%	76	23.5%	230	70.6%
	%	67.0%		33.0%			
Totals		181	55.5%	145	44.5%	326	100.0%

$Chi^2 = 39.8$ ($p = 2.3 \times 10^{-9}$) 11 July 2006.

end points that may be relevant to health" (probability of industry-funded study reporting at least one significant result is 0.11, CI: 0.02–0.78) [37].

Financial bias is pervasive across all fields of science. It is sufficiently pervasive that books have been written on the subject and science journals have brought it to the attention of their readers. A search for books about "Funding Bias in Science" at Amazon.com found 86 titles [38].

In a review of the book 'Science in the Private Interest: Has the Lure of Its Profits Corrupted Biomedical Research?' by Sheldon Krimsky, Dr. Roger Porter wrote, "The major theme of this superb book, therefore, is the degradation of the academic scientist, who is lured to the pecuniary gains offered by industry and now asks the scientific questions posed by industry instead of independently pursuing scientific investigation of public needs." [39].

A news report in the British Medical Journal reported, "Four German public health scientists have been publicly criticised in Der Spiegel magazine for accepting funding from the tobacco industry in return for supporting tobacco friendly research projects and policies in the 1980s." [40].

A substantial portion of the Interphone study funding comes from the cellphone industry. For European studies, industry has provided more than €3.2 million ($5.1M) [27], another $1 million came from the Canadian Wireless Telecommunications Association [41] and it is unknown if industry funding has been provided for studies in Japan, Australia and New Zealand.

In addition to the €3.2 million the Interphone Exposure Assessment Committee received funding from the UK Network Operators (O2, Orange, T-Mobile, Vodafone, '3') and French Network Operators (Orange, SFR, Bouygues) [36]. At least one member of this Committee is employed by a cellphone company: Dr. Joe Wiart from France Telecom [20].

Beyond the €3.2 million available to the European Interphone studies, the French study [12] received funding from "Orange, SFR, Bouygues Télécom." [42]; the UK study received funding from O2, Orange, T-Mobile, and Vodafone, and [13]; the Danish study received funds from the for-profit International Epidemiology Institute (IEI). The source of the IEI funds is not stated [9].

Funding for the 5-country Interphone study of acoustic neuroma also came from O2, Orange, T-Mobile, Vodafone, '3' [18].

The Muscat et al. studies [2,4] received around $600,000 from the Cellular Telecommunication Industry Association (CTIA) via the organization CTIA created and funded, Wireless Technology Research (WTR) [43]. For the Auvinen et al. study "Finnish mobile phone manufacturers contributed to the funding for the TEKES research program." [5].

4. Increased risk Interphone laterality findings

So far the discussion had pertained to the aggregate results of the 11 Interphone brain tumor studies. It is important to note that when significant findings of risk were examined for ≥10 years of cellphone use it was found that 2 studies had 3 significantly increased risk results (all 3 were for ipsilateral use). The Swedish Lönn et al. acoustic neuroma study had two significant results showing an increased risk: OR = 3.9 (CI: 1.6 to 9.5) for ≥10 years since first ipsilateral use (based on 12 cases), and OR = 3.1 (CI: 1.2 to 8.4) for ≥10 years of ipsilateral use (based on 9 cases) [6]. The UK Hepworth et al. glioma study reported OR = 1.24 (CI: 1.02 to 1.52) for ≥10 years of ipsilateral use (based on 278 cases) [13].

If we examine Table 3 there is little difference between the parameters of these studies relative to the weighted average of all 11 studies. The Lönn et al. acoustic neuroma study had the third smallest control refusal rate (27.9%), yet the Hepworth et al. glioma study had the highest control refusal rate (65.5%).

When the weighted averages are calculated without the Lönn (2005) and Hepworth studies (see Table 3) the Dx years and the % of cases who used a cellphone for >10 years remained unchanged. However, the % of controls who refused to participate is 33.4% (from 40.7%). This is because the Hepworth study has the hightest number of controls of any of the 11 studies (1716 controls, 24% of all controls) and the highest control refusal rate (65.5%) of the 11 studies.

Possibly the increased risk of brain tumors could be the result of laterality recall bias. Yet, as would be expected the ipsilateral ORs are greater than the contralateral ORs in all

3 findings suggesting there was little or no laterality recall bias.

Of the remaining 9 Interphone brain tumor studies, 3 studies had no cases that had used a cellphone for ≥10 years, and 3 of the studies with cases that had used a cellphone for ≥10 years did not report laterality results [7,9,10]. The Lönn et al. study did find non-significant glioma increased risks for ≥10 years since first ipsilateral use and for ≥10 years duration of "regular" ipsilateral use (OR = 1.6, CI: 0.8 to 3.4, $p = 0.19$, based on 15 cases, and OR = 1.8, CI: 0.8 to 3.9, $p = 0.14$, based on 14 cases, respectively), and similar increased meningioma risks were found for ≥10 years of ipsilateral use and ≥10 years duration of "regular" ipsilateral use (OR = 1.3, CI: 0.5 to 3.9, based on 5 cases, and OR = 1.4, CI: 0.4 to 4.4, based on 4 cases, respectively) [8]. Every Interphone Odds Ratio for ≥10 years of ipsilateral cellphone use reported an increased risk (OR > 1.0).

This suggests that when the two highest exposures reported in the Interphone study are combined (≥10 years of use and ipsilateral use), the resultant increased risk offsets the overall systemic protective skew resulting from the Interphone Protocol's flaws, and an increased risk is found in spite of the systemic protective skew. If true, whatever the reported risk, the actual risk (flaws removed) is larger.

5. The independently funded Swedish studies led by Dr. Lennart Hardell

These studies had virtually no industry funding and were entirely within a single-country: Sweden. Table 8 compares both sets of studies. Clearly the Interphone studies have more cases than the Hardell studies. However, the Hardell studies have more cases that used a cellphone for 10 or more years. Almost certainly, the larger number of long-term users is because of the considerably longer diagnosis eligibility range (range of brain tumor diagnosis dates when cases are eligible to participate in a study).

Because selection bias increases as the control refusal rate increases, the substantially smaller control refusal rate in the Swedish studies mitigates against any significant selection bias while the 3.6-fold larger Interphone studies control refusal rates enhances the problem of selection bias.

The Swedish studies, with some exceptions: did not examine risks in regions exposed to the cellphone's radiation plume (flaw 8), excluded cases who had died or were too ill to be interviewed (flaw 9), and did not use subjects' billing records (flaw 10). The Interphone studies had all 11 flaws but did include a portion of the cases that had died or were too ill to be interviewed (flaw 9).

In contrast to the Interphone studies results, which appear to be incredulous (i.e., use of a cellphone protects the user from a brain tumor), the Hardell team results are internally consistent if wireless phones (cellphones and/or cordless phones) use is a risk of brain tumors.

- The higher the cumulative hours of use, the higher the risk [35];
- The higher the radiated power, the higher the risk [44];
- The higher the number of years since first use, the higher the risk [35];
- The higher the exposure (tumor on the same side of the head where the cellphone or cordless phone was held), the higher the risk [25,26], and;
- The younger the user, the higher the risk [29].

6. Role of industry

There has been a long history of industry using "science" to counter findings of risk by industry independent scientists [45]. Over many decades multiple industries have perfected a series of techniques used to diminish or delay effective action that is perceived as harmful to their interests [45].

If we examine, the history of tobacco, ionizing radiation, asbestos, and more recently cellphones, we see there has been an extraordinarily long time between first warnings (followed by many more warnings) and the eventual Public Health acknowledgement that there is a problem (Tobacco: 1856–1964; Ionizing Radiation: 1896–1998; Asbestos: 1911–1996; Cellphones: 1993–?) [46].

6.1. Insufficient funding

Arguably, inadequate funding of research projects is the most common reason why previous studies had been unable to detect what was later seen as an obvious risk. Given insufficient funding, many naïve researchers accept the grant and proceed with the best possible study given the financing provided. Here are two examples.

At the 2005 meeting of the Bioelectromagnetics Society a study was presented of rats exposed to cellphone radiation.

Table 8
Comparison of Interphone studies and Swedish Hardell studies.

Study	Total cases	≥10 years of use cases	Controls	Participation refusal rate		Dx eligibility range years	Industry funding	Identified flaws
				Cases	Controls			
Interphone[a]	4378	172	7229	14.1%[b]	40.7%[b]	2.69[b]	$6.1M+	1 to 11
Hardell	2159	289	2162	11.2%[c]	11.3%	6.00	$0	8, 9, 10

[a] Based on 11 single-country Interphone studies published to date (March 2009).
[b] Weighted-average of 11 single country Interphone studies published to date (March 2009).
[c] Weighted-average of two pooled studies, "benign" and malignant brain tumors.

The study used 13 rats in two groups: 5 for cellphone radiation effects on rat brains, and 8 for cellphone radiation effects on rat skin [47]. As would be expected, with such a small group of animals, no effects were found. When the presenter was asked why she had used so few animals, she said France Telecom had not given her sufficient funding to use more animals.

A second example, is the Interphone study, with more than €3.2 million ($5.1M) of industry money for European research teams [27], and another $1 million from the Canadian Wireless Telecommunications Association (CWTA) [40]. The overwhelming majority of significant Interphone study findings found cellphone use *protects* the user from brain tumors. As discussed above, adequate funding could have eliminated or substantially mitigated the numerous flaws that can account for this incredulous result.

7. Potential public health impact

What is the potential public health impact if cellphone use induces brain tumors? The answer is we do not know, but it is possible to make a rough estimate based on information we have. We can use the CTIA cellphone subscriber data by year [48], and assume that there is a 30-year time delay between first cellphone use and the diagnosis of a brain tumor (latency time). We can also assume that 10% of long-term cellphone users will be diagnosed with a brain tumor, similar to 10% of long-term smokers diagnosed with lung cancer. The result is Fig. 1, which estimates the potential number of cellphone-induced brain tumors by year in the United States. Since Fig. 1 is based on a mathematic model, it can be legitimately challenged (even by this author), and the numerical assumptions adjusted. However, this author finds the shape of the graph, a long time delay followed by a rapid increase in brain tumors, to be highly credible.

As can be seen in Fig. 1, for many years, only a minute number of cellphone-induced brain tumors would be predicted each year (invisible on the scale of the graph). By 2004, the most recent year US brain tumor diagnosis data is available there remains an imperceptible ~1900 cellphone-induced brain tumors. In 2004 the model calculates there would be about 1900 cellphone-induced brain tumors out of ~50,000 brain tumors diagnosed that year [49]. By 2009 an increase can be seen in the graph (but the incidence of brain tumors would not be reported by the government until 2013). After 2009 there is a very rapid increase. The model predicts there will be ~380,000 cellphone-induced brain tumors in 2019.

This would overwhelm the United States public health system. The cost of treating brain tumor patients is on the order of $250,000 per patient [50]. This translates to a $9.5B cost in 2019. Since this would also require roughly a 7-fold increase in neurosurgeons within the next 11 years, surgery for the vast majority of cases would not be an option, so the estimated $9.5B cost would be far less due to lack of treatment resources.

8. Precautionary Principle

Simply put, the Precautionary Principle (PP) is a policy that says if there is some evidence that a problem may exist and low, or no-cost remedial actions are possible, then these actions should be undertaken. Colloquially, we say, "Better safe than sorry." If cellphones induce brain tumors the potential public health costs are large. There is also a simple action that can reduce the absorbed cellphone radiation by several orders of magnitude.

Cellphone radiation decreases as the square of the distance from the phone. As a result even small changes in distance

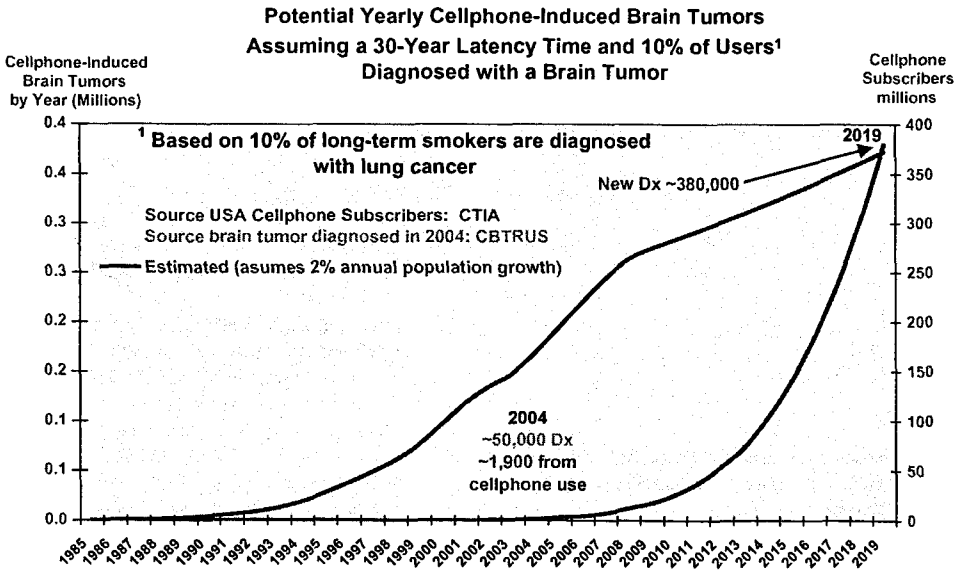


Fig. 1. Long-delay followed by sudden onset of brain tumor epidemic.

have a dramatic effect. For example, when the speaker on the cellphone is placed to the ear, the cellphone is 2 mm from the head and if the cellphone is held 200 mm (100 times) from the head, this change in distance would result in a 10,000-fold reduction in the radiation absorbed by the head.

With use of a headset (not a wireless headset) connected to a cellphone the cellphone is not held directly against the ear and thus the absorbed cellphone radiation could be reduced by several orders of magnitude.

An appropriate PP action would be to mandate cellphone manufacturers to remove the existing cellphone speaker that is placed to the ear and replace it with a headset directly connected to the cellphone. The cost would be near zero (potentially a net cost savings): remove one cellphone speaker—add another speaker (AKA headset).

9. Conclusions

The industry-funded Interphone study has assured the public there is no risk of brain tumors from cellphone use. Yet, a closer analysis of the data leads to the incredulous conclusion that cellphone use protects the user from brain tumors ($p = 6.2 \times 10^{-20}$). A more likely explanation of the data is that the studies were flawed and that there is a link between cellphone use and brain tumors. The Swedish team studies, independent of industry funding, have reported increased brain tumor risk from cellphone use and cordless phone use.

The long history of corporate funded "science" delaying effective action against toxic agents, in some cases up to 100 years, argues convincingly for application of the Precautionary Principle. This is especially true in light of the potentially enormous public health impact should cellphones be shown to cause brain tumors.

The Precautionary Principle clearly applies in this case, since the problem is possible but not certain, and low cost ameliorating actions are easily implemented by industry. With over 3 billion people using cellphones, and with children among the heaviest users, it is time for governments to mandate precautionary measures to protect their citizens.

Conflicts of interest

None.

References

[1] Hardell, et al., Case–control study on radiology work, medical X-ray investigations, and use of cellular telephones as risk factors for brain tumors, MedGenMed. 2 (May 4 (2)) (2000) E2.

[2] Muscat, et al., Handheld cellular telephone use and risk of brain cancer, J. Am. Med. Assoc. 284 (December 20 (23)) (2000).

[3] Inskip, et al., Cellular-telephone use and brain tumors, N. Engl. J. Med. 344 (January 11 (2)) (2001) 79–86.

[4] Muscat, et al., Handheld cellular telephones and risk of acoustic neuroma, Neurology 58 (2002) 1304–1306.

[5] Auvinen, et al., Brain tumors and salivary gland cancers among cellular telephone users, Epidemiology 13 (May (3)) (2002) 356–359.

[6] Lönn, et al., Mobile phone use and the risk of acoustic neuroma, Epidemiology 15 (November (6)) (2004).

[7] Christensen, et al., Cellular telephone use and risk of acoustic neuroma, Am. J. Epidemiol. 159 (2004) 277–283.

[8] Lönn, et al., Long-term mobile phone use and brain tumor risk, Am. J. Epidemiol. 161 (2005) 526–535.

[9] Christensen, et al., Cellular telephones and risk for brain tumors. A population-based, incident case–control study, Neurology 64 (2005) 1189–1195.

[10] Schüz, et al., Cellular phones, cordless phones, and the risks of glioma and meningioma (Interphone Study Group, Germany), Am. J. Epidemiol. 163 (March 15 (6)) (2006) 512–520.

[11] T. Takebayashi, S. Akiba, K. Kikuchi, et al., Mobile phone use and acoustic neuroma risk in Japan, Occup. Environ. Med. 63 (2006) 802–807.

[12] Hours, et al., Téléphone mobile, risque de tumeurs cérébrales et du nerf vestibuloacoustique: l'étude cas-témoins INTERPHONE en France (Cell Phones and Risk of brain and acoustic nerve tumours: the French INTERPHONE case–control study), Revue d'Épidémiologie et de Santé Publique (2007).

[13] Hepworth, et al., Mobile phone use and risk of glioma in adults: case–control study, BMJ 332 (April 15 (7546)) (2006) 883–887.

[14] Klaeboe, et al., Use of mobile phones in Norway and risk of intracranial tumours, Eur. J. Cancer Prev. 16 (April (2)) (2007) 158–164.

[15] Takebayashi, et al., Mobile phone use, exposure to radiofrequency electromagnetic field, and brain tumour: a case–control study, Br. J. Cancer 98 (2008) 652–659.

[16] Schlehofer, et al., Environmental risk factors for sporadic acoustic neuroma (Interphone Study Group, Germany), Eur. J. Cancer 43 (July (11)) (2007) 1741–1747.

[17] Lahkola, et al., Meningioma and mobile phone use—a collaborative case–control study in five North European countries, Int. J. Epidemiol. (2008) August 2 [Epub ahead of print].

[18] Schoemaker, et al., Mobile phone use and risk of acoustic neuroma: results of the Interphone case–control study in five North European countries, Br. J. Cancer (2005) 1–7.

[19] Lahkola, et al., Mobile phone use and risk of glioma in 5 North European countries, Int. J. Cancer 120 (2007) 1769–1775.

[20] E. Cardis, M. Kilkenny, INTERPHONE, International Case Control Study of Tumours of the Brain and Salivary Glands, Protocol, rev. 1, International Agency for Research on Cancer, Lyon, France 2001, IARC internal report 01/002.

[21] S. Milham, Personal communication, 18 August 2008.

[22] S. Sadetzki, A. Chetrit, L. Freedman, Long-term follow-up for brain tumor development after childhood exposure to ionizing radiation for tinea capitis, Radiat. Res. 163 (2005) 424–432.

[23] W. Weiss, Cigarette smoking and lung cancer trends. A light at the end of the tunnel? Chest 111 (May (5)) (1997) 1414–1416.

[24] C. Bianchi, L. Giarelli, G. Grandi, et al., Latency periods in asbestos-related mesothelioma of the pleura, Eur. J. Cancer Prev. 6 (April (2)) (1997) 162–166.

[25] Hardell, et al., Pooled analysis of two case–control studies on the use of cellular and cordless telephones and the risk of benign brain tumours diagnosed during 1997–2003, Int. J. Oncol. 28 (2006) 509–518.

[26] Hardell, et al., Pooled analysis of two case–control studies on use of cellular and cordless telephones and the risk for malignant brain tumours diagnosed in 1997–2003, Int. Arch. Occup. Environ. Health 79 (September (8)) (2006) 630–639.

[27] History of Mobile Phone Usage Mobile Operators Association UK (2008), http://www.mobilemastinfo.com/information/history.htm, accessed 20 November 2008.

[28] Elizabeth Cardis (in response to questions), Plenary Session II, Epidemiology Studies on Cellular Telephones Use and the Risk of Brain

Tumors, Bioelectromagnetics Society Meeting, San Diego, CA, June 9, 2008.
[29] Hardell, et al., Cellular and cordless telephone use and the association with brain tumors in different age groups, Arch. Environ. Health 59 (March (3)) (2004) 132–137.
[30] Choi, et al., Case–control studies on human effects of wireless phone RF in Korea, in: BEMS 28th Annual Meeting, Cancún, Mexico, 2006.
[31] Lönn, et al., Output power levels from mobile phones in different geographical areas; implications for exposure assessment, Occup. Environ. Med. 61 (2004) 769–772.
[32] Repacholi, et al., Lymphomas in E mu-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields, Radiat. Res. 147 (5) (1997) 631–640.
[33] Cardis, et al., Distribution of RF energy emitted by mobile phones in anatomical structures of the brain, Phys. Med. Biol. 53 (2008) 2771–2783.
[34] Eberhardt, et al., Blood–brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones, Electromagn. Biol. Med. 27 (3) (2008) 215–229.
[35] Mild, et al., Pooled analysis of two Swedish case–control studies on the use of mobile and cordless telephones and the risk of brain tumours diagnosed during 1997–2003, Int. J. Occup. Safety Ergon. (JOSE) 13 (1) (2007) 63–71.
[36] Vrijheid, et al., Validation of short term recall of mobile phone use for the Interphone study, Occup. Environ. Med. 63 (April (4)) (2006) 237–243.
[37] Huss, et al., Source of funding and results of studies of health effects of mobile phone use: systematic review of experimental studies, Environ. Health Perspect. 115 (2007) 1–4.
[38] http://www.amazon.com/s/ref=nb_ss_b?url=search-alias%3Dstripbooks&field-keywords=Funding+Bias+in+Science&x=21&y=16, accessed 30 November 2008.
[39] Neurology Today, vol. 4(9), September 2004, pp. 56, 57, 58.
[40] A. Tuffs, Public health scientists accused of soft peddling the dangers of passive smoking after taking grants from tobacco related organizations, BMJ 331 (9 July) (2005) 70.
[41] Linda Diebel, Ottawa linked to cellphone lobbyists, Toronto Star, August 2, 2008, http://www.thestar.com/printArticle/471613, accessed 2 August 2008.
[42] Cardis, et al., The INTERPHONE study: design, epidemiological methods, and description of the study population, Eur. J. Epidemiol. 22 (9) (2007) 647–664.
[43] G. Carlo, Personal communication, 30 November 2008.
[44] Hardell, et al., Use of cellular telephones and brain tumour risk in urban and rural areas, Occup. Environ. Med. 62 (2005) 390–394.
[45] D. Michaels, Doubt Is Their Product How Industry's Assault on Science Threaten Your Health, Oxford University Press, 2008.
[46] D. Gee, V.S. Guedes, Late lessons from early warnings: the precautionary principle 1896–2000, Environmental issue report no. 22, European Environment Agency, Copenhagen, Denmark, 2001.
[47] Poulletier de Gannes, et al., In vivo studies of the effects of GSM microwave exposure on heat shock protein expression, BioEM 2005—Joint BEMS/EBEA Meeting, Dublin, Ireland, 2005 (http://www.bioelectromagnetics.org/pubs.php?PHPSESSID=90b6cfbb0a467a640a6f09b21a5f98dc, accessed 8 August 2008).
[48] CTIA Semi-Annual Wireless Industry Survey (http://files.ctia.org/pdf/CTIA_Survey_Mid_Year_2008_Graphics.pdf), accessed 14 November 2008.
[49] CBTRUS, Supplement Report, Primary Brain Tumors in the United States, 2004, Published by the Central Brain Tumor Registry of the United States, Hinsdale, IL, 2008.
[50] Fisher, et al., Biologic and Environmental Risk Factors for Childhood Brain Tumors: The California Childhood Brain Tumor Study (CCBTS), 2004.

ELSEVIER

Pathophysiology 16 (2009) 149–156

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Review

Long-term exposure to magnetic fields and the risks of Alzheimer's disease and breast cancer: Further biological research

Zoreh Davanipour[a,*], Eugene Sobel[b]

[a] *Northwestern University, Feinberg School of Medicine, Chicago, IL, United States*
[b] *Friends Research Institute, Los Angeles, CA, United States*

Received 1 November 2008; accepted 30 January 2009

Abstract

Objective: Extremely low frequency (ELF) and radio frequency (RF) magnetic fields (MFs) pervade our environment. Whether or not these magnetic fields are associated with increased risk of serious diseases, e.g., cancers and Alzheimer's disease, is thus important when developing a rational public policy. The Bioinitiative Report was an effort by internationally recognized scientists who have spent significant time investigating the biological consequences of exposures to these magnetic fields to address this question. Our objective was to provide an unbiased review of the current knowledge and to provide our general and specific conclusions. **Results:** The evidence indicates that long-term significant occupational exposure to ELF MF may certainly increase the risk of both Alzheimer's disease and breast cancer. There is now evidence that two relevant biological processes (increased production of amyloid beta and decreased production of melatonin) are influenced by high long-term ELF MF exposure that may lead to Alzheimer's disease. There is further evidence that one of these biological processes (decreased melatonin production) may also lead to breast cancer. Finally, there is evidence that exposures to RF MF and ELF MF have similar biological consequences. **Conclusion:** It is important to mitigate ELF and RF MF exposures through equipment design changes and environmental placement of electrical equipment, e.g., AC/DC transformers. Further research related to these proposed and other biological processes is required.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Extremely low frequency (ELF); Magnetic fields (MFs); Amyloid beta (Aβ); Melatonin; Alzheimer's disease (AD)

Contents

1. Introduction 150
2. Epidemiologic studies presented in the Bioinitiative Report related to Alzheimer's disease and breast cancer 150
   2.1. Alzheimer's disease 150
   2.2. Breast cancer 150
3. Biological hypotheses relating ELF MF exposure to Alzheimer's disease and breast cancer 150
   3.1. ELF MF exposure and peripheral and brain production of amyloid beta (Fig. 1) 151
   3.2. Melatonin—background 151
   3.3. Low melatonin production and Alzheimer's disease 152
   3.4. Low melatonin production and breast cancer 152
4. Discussion and future research 153
   4.1. Epidemiologic studies 153
   4.2. ELF and/or RF MF exposure mitigation 154
   4.3. Biological mechanisms/experimental medicine research 154
   Acknowledgement 154
   References 154

* Corresponding author.
E-mail address: zdavani@earthlink.net (Z. Davanipour).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.005

1. Introduction

In this review, we emphasize (a) two proposed biological models "explaining" the apparent relationship between high, long-term exposure to extremely low frequency (ELF) magnetic fields (MFs) and Alzheimer's disease (AD), one of which also relates to breast cancer and (b) areas of biological research needed to confirm or refute these models. Prior to this discussion, we provide the conclusions from our detailed review chapter (Section 12: Davanipour and Sobel [1]) in the Bioinitiative Report [2] related to epidemiologic research, which initially identified these relationships. We refer the reader to Section 12 and supporting, peer-reviewed papers for details of the epidemiologic studies discussed in that section. Other papers in this issue of Pathophysiology (e.g., on the stress response and DNA strand breaks) demonstrate that exposures to ELF MF and radio frequency (RF) MF often have the same biological consequences.

2. Epidemiologic studies presented in the Bioinitiative Report related to Alzheimer's disease and breast cancer

The conclusions reached from our detailed review of the literature in Section 12 in the Bioinitiative Report (see references for URL) on long-term significant ELF MF exposure and Alzheimer's disease and breast cancer are provided below [1]. The section references below refer to sub-sections of Section 12 of the Bioinitiative Report.

Melatonin production (Section II). Eleven of the 13 published epidemiologic residential and occupational studies are considered to provide (positive) evidence that high long-term ELF MF exposure can result in decreased melatonin production. The two negative studies had important deficiencies which may certainly have biased the results. Thus, there is sufficient evidence to conclude that long-term relatively high ELF MF exposure can result in a decrease in melatonin production. It has not been determined to what extent personal characteristics, e.g., medications, interact with ELF MF exposure in decreasing melatonin production.

2.1. Alzheimer's disease

Section 12 of the Bioinitiative Report provides the details of the following conclusions.

- There is initial evidence that (i) a high level of peripheral amyloid beta, generally considered the primary neurotoxic agent when aggregated, is a risk factor for AD and (ii) medium to high MF exposure can increase peripheral amyloid beta. High brain levels of amyloid beta are also a risk factor for AD and medium to high MF exposure to brain cells likely also increases these cells' production of amyloid beta (Section IIIA).
- There is considerable *in vitro* and animal evidence that melatonin protects against AD. Therefore, it is certainly possible that low levels of melatonin production are associated with an increase in the risk of AD (Section IIIB).
- There is strong epidemiologic evidence that long-term exposure to ELF MF is a risk factor for AD. There are seven studies of ELF MF exposure and AD that met our inclusion criteria. Six of these studies are more of less positive and only one is negative. The negative study has a serious deficiency in ELF MF exposure classification which results in subjects with rather low exposure being considered as having significant exposure. Several published studies were excluded from further consideration due to serious deficiencies, primarily diagnostic inaccuracy (e.g., use of death certificates for diagnosis of AD) and/or serious exposure assessment problems. These latter studies likely had risk estimated seriously biased towards the null hypothesis of no risk. It should be noted, however, that even some of these studies were positive (Sections IIIC and IIID).

2.2. Breast cancer

There is sufficient evidence from *in vitro* and animal studies, from human biomarker studies, from occupational and light at night case-control studies, and the only two longitudinal studies with appropriate collection of urine samples to conclude that high ELF MF exposure may certainly be a risk factor for breast cancer (Section IV). Note that at the time the Bioinitiative Report was made public, there was only one longitudinal study with appropriate collection of urine samples. There are now two such studies [3,4].

Seamstresses. Seamstress is, in fact, one of the most highly ELF MF exposed occupations, with exposure levels generally well above 10 mG over a significant proportion of the workday. Seamstresses have been consistently found to be at higher risk of Alzheimer's disease and breast cancer. This occupation deserves specific attention in future studies. We are unaware of any measurements of RF MF among seamstresses (Section V and throughout Section 12).

3. Biological hypotheses relating ELF MF exposure to Alzheimer's disease and breast cancer

Two biological hypotheses are discussed. The first one relates ELF MF exposure to increased amyloid beta (Aβ) production and subsequent development of AD. The second one relates ELF MF exposure to decreased melatonin production. Decreased melatonin production appears to have differing deleterious consequences related to AD and breast cancer development.

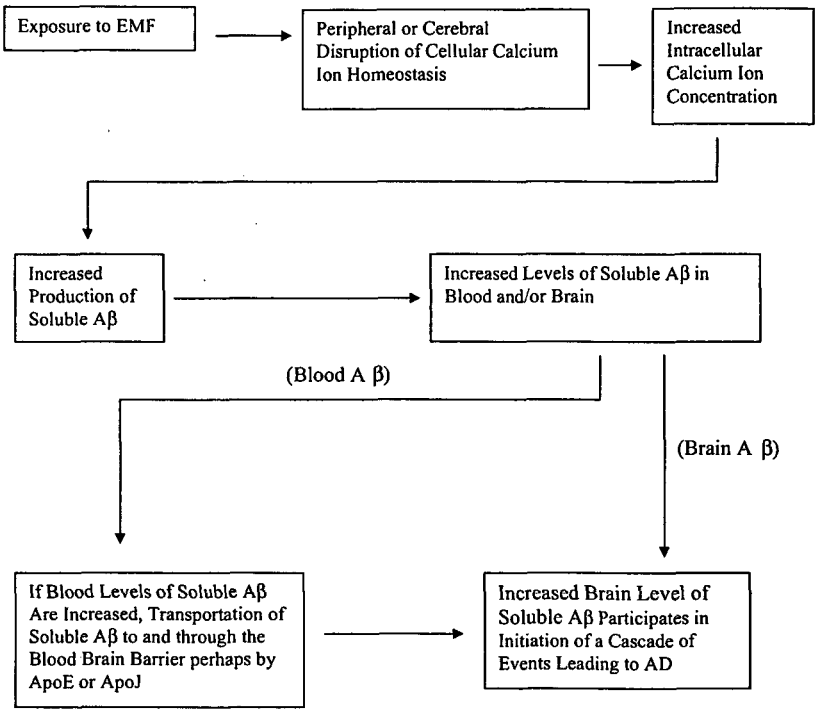


Fig. 1. Hypothesized biological pathway from MF exposure to AD Development (from Sobel and Davanipour [5]).

3.1. ELF MF exposure and peripheral and brain production of amyloid beta (Fig. 1)

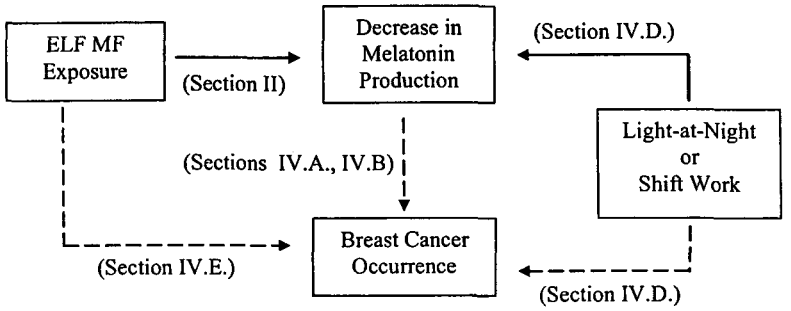
The ELF MF exposure and increased amyloid beta hypothesis was developed by Sobel and Davanipour as a result of our initial findings that long-term ELF MF occupational exposure was a risk factor for AD [5] (see Fig. 1). Seamstress was the most common occupation among subjects with AD in the five databases we investigated [6–8]. ELF MF exposure among seamstresses had not been measured prior to our 1995 study [6]. Beginning in 1994, we measured a very large number of seamstresses working in either a factory setting or individually. Their exposures were very high, particularly when using an industrial sewing machine. The highest exposures were, however, not to the brain, because the motor on industrial machines is located at the knees. The motor or AC/DC transformer in home sewing machines is in the machine arm located near the operator's chest and right arm. This peripheral exposure led us to consider how peripheral ELF MF exposure might be associated with development of amyloid plaques in the brain.

Our biologically plausible hypothesis relating MF exposure to AD is based on the independent work of many researchers in several different fields. Details and references are provided in Sobel and Davanipour [5]. Briefly, the hypothesized process involves increased peripheral or brain production of Aβ as a result of MF exposure causing voltage-gated calcium ion channels to be open longer than normal. This results in abnormally high intracellular levels of calcium ions which in turn results in the production of Aβ. The resulting Aβ is quickly secreted into the blood. If peripheral, the Aβ is then transported to and through the blood–brain barrier, perhaps best chaperoned by the ε4 isoform of apolipoprotein E (apoE). (Note that this might be one reason why the ε4 isoform is a risk factor for AD.) Fig. 1 provides a schematic outline of the hypothesis. Each step in the proposed pathway is supported by *in vitro* studies.

At the time of publication of this hypothesis, no human studies related to this hypothesis had been conducted. There are now two groups that have published relevant studies, without apparently any knowledge of our hypothesis—or at least no reference to the hypothesis: (1) high levels of peripheral $A\beta_{1-42}$, the more neurotoxic version of Aβ, has been found to be a risk factor for AD [9,10]; acute exposure to ELF MF increases peripheral Aβ [11]. Details may also be found in the Bioinitiative Report (Section IIIA) [1].

3.2. Melatonin—background

Melatonin is found in every cell of the body and readily crosses the blood–brain barrier. It scavenges reactive oxygen species (ROS) at both physiologic and pharmacologic concentrations. In the literature, "physiologic" refers to blood level concentrations of melatonin, while "pharmacologic" indicates 2–3 orders of magnitude higher concentration. Recently, intracellular levels of melatonin, especially within the nucleus, have been shown to be naturally at "pharmacologic" levels for all cellular organelles studied to date [12,13].



Note: Dashed lines indicate studies directly relating ELF MF exposure, light-at-night or shift work, or lower melatonin production to breast cancer occurrence. Section references refer to Section 12 of the Bioinitiative Report [1].

Fig. 2. Outline of the evidence that ELF MF exposure causes breast cancer through decreases in melatonin production—with section references to Section 12, Bioinitiative Report [1]. Note: Dashed lines indicate studies directly relating ELF MF exposure, light-at-night or shift work, or lower melatonin production to breast cancer occurrence.

3.3. Low melatonin production and Alzheimer's disease

Numerous *in vitro* and animal studies indicate that melatonin may be *protective* against AD and thus low or lowered melatonin production may be a risk factor for AD. These studies have found that melatonin has the following effects:

- Inhibition of the neurotoxicity and cytotoxicity of Aβ, including in mitochondria [14–19];
- Inhibition of the formation of β-pleated sheet structures and Aβ fibrils [20–25];
- Reversal of the profibrillogenic activity of apolipoprotein E ε4, an isoform conferring increased risk of AD [21];
- Inhibition of the oxidative stress *in vitro* and in transgenic mouse models of AD, if given early [23,26,27], but not necessarily if given to old mice [28];
- Increase in survival time in mouse models of AD [23];
- Reduction of oxidative stress and of proinflammatory cytokines induced by $A\beta_{1-40}$ in rat brain *in vitro* and *in vivo* [29–31];
- Decrease of the prevalence of $A\beta_{1-40}$ and $A\beta_{1-42}$ in the brain in young and middle aged mice [32];
- Improvement of memory and learning in rat models of AD pathology [33,34], but not necessarily in Aβ-infused rat models [35].

Note that transgenic mouse models of AD mimic senile plaque accumulation, neuronal loss, and memory impairment. There have been several reviews, e.g., [36–39]. Thus, chronic low levels of melatonin production may be etiologically related to AD incidence [40].

3.4. Low melatonin production and breast cancer

See Fig. 2 for a diagram of the discussed relationships between ELF MF exposure and breast cancer risk.

In vitro studies related to prevention of oxidative damage. Well over 1000 publications have found that melatonin neutralizes hydroxyl radicals and reduces oxidative damage. For reviews see Tan et al. [41] and Peyrot and Ducrocq [42]. Melatonin has also been shown to act synergistically with vitamin C, vitamin E and glutathione [43] and stimulates the antioxidant enzymes superoxide dismutase, glutathione peroxidase and glutathione reductase [44]. Furthermore,

- melatonin neutralizes hydroxyl radicals more efficiently than does reduced glutathione [45,46];
- melatonin reduces oxidative damage to macromolecules in the presence of free radicals [47,48] due at least to its free radical scavenging properties [49];
- melatonin increases the effectiveness of other antioxidants, e.g., superoxide dismutase, glutathione peroxidase, and catalase [50–54];
- melatonin has protective effects against ultraviolet and ionizing radiation [55–57];
- melatonin has been found to be a more potent protector from oxidative injury than vitamin C or vitamin E (micromoles/kg) (for a review of the evidence, see: Tan et al. [43];
- melatonin was also found *in vitro* to scavenge peroxyl radicals more effectively than vitamin E, vitamin C or reduced glutathione [58], although melatonin is not a very strong scavenger of peroxyl radicals [49].

Animal studies of melatonin and mammary tumor prevention. Several studies have found that melatonin inhibits the incidence of mammary tumors in laboratory animals either prone to such tumors or exposed to a carcinogen (e.g., [50–63]). Tan et al. [64,65] found that melatonin at both physiological and pharmacological levels protected Sprague–Dawley rats from safrole induced liver DNA adduct formation. Melatonin and retinoic acid appear to act synergistically in the chemoprevention of animal model tumors [66] and *in vitro* systems [67].

Melatonin prevents oxidative DNA damage by estradiol and radiation. Karbownik et al. [68] found that melatonin

protects against DNA damage in the liver and kidney of male hamsters caused by estradiol treatment. Several studies have found that laboratory animals are protected by melatonin from lethal doses of ionizing radiation (e.g., [69–71]). Vijayalaxmi et al. [70] and Karbownik et al. [71] also investigated markers of oxidative DNA damage and found significant decreases in these markers in the melatonin treated animals.

Melatonin: Scavenger of •OH and Other ROS. Melatonin is a powerful, endogenously produced scavenger of reactive oxygen species (ROS), particularly the hydroxyl radical (•OH). Other ROS which melatonin scavenges include hydrogen peroxide (H_2O_2), nitric oxide (NO•), peroxynitrite anion ($ONOO^-$), hypochlorous acid (HOCl), and singlet oxygen ($^1O_2$) [50,72–75]. •OH is produced at high levels by natural aerobic activity. ROS are also produced by various biological activities or result from certain environmental and lifestyle (e.g., smoking) exposures. •OH is the most reactive and cytotoxic of the ROS [76]. •OH appears not to be removed by antioxidative enzymes, but is only detoxified by certain direct radical scavengers such as melatonin [77].

4. Discussion and future research

Other papers in this special issue of Pathophysiology provide evidence that RF MF exposure and ELF MF exposure may have similar biological consequences.

We primarily limit our discussion of future research to studies in humans with experimental medicine components, emphasizing the latter. However, we initially discuss limiting exposures.

It should be noted that ELF MF exposure may also be associated with other cancers. This may be because of the decrease in melatonin production and melatonin's varying antioxidant, anti-inflammation, and immune response enhancement properties.

4.1. Epidemiologic studies

The incidence rates of Alzheimer's disease and breast cancer are increasing. These increases are certainly in part due to our living longer, at least for AD, if not better lives. However, environmental exposures are likely to play important roles. At the same time, ELF and RF MF exposure is becoming more and more common in our world. In our three published studies of MF and AD, approximately 7.4–12.0% of the cases and 3.4–5.3% of the controls had primary occupations associated with medium or high ELF MF exposure [6–8]. Many more subjects may have had exposures from sources generally not identified in epidemiologic studies, because individualized 'on-site' exposure assessment is usually not feasible. We give two examples coming from 'onsite' inspections we have performed: a subject who had developed amyotrophic lateral sclerosis (ALS) had spent many years with a 75 mG ELF MF exposure due to having his foot on a deadbolt lock/unlock foot devise for his office door under his desk; a subject who had developed AD who spent over 25 years sitting at his home desk for at least 4 h per day in a chair backed up to a wall with a fuse box directly on the other side of the wall which produced a very high ELF MF exposure to his back and head. (Note that there is also significant epidemiologic evidence that ELF MF exposure is a risk factor for ALS.) The frequencies of such exposures in studies are unknown.

As is often the case, more research is required. However, the designs of this future research should be informed and directed by the results of previous research. Future epidemiologic studies should use subjects for whom it is unequivocally known that the ELF MF and/or RF MF exposure is high and matched subjects for whom such exposure is known to be low. Matching criteria should include age, gender, and residential environment so as to at least partially exclude other exposures.

There should be additional studies related to the levels of production of peripheral amyloid beta, particularly $A\beta_{1-42}$, and melatonin, on the one hand, and both MF exposure and the risk of AD, on the other hand. Such studies need to be able to investigate the possible associations between peripheral amyloid beta and melatonin levels and both earlier/concurrent MF exposure and subsequent development of AD. Similar studies need to be carried out for breast cancer, excluding the amyloid beta component. This effort will likely require both retrospective and longitudinal studies. There are only two known longitudinal studies [3,4] which collected urine samples at baseline so that overnight premorbid melatonin production was reliably estimated. These studies found an association between low melatonin production and breast cancer. These studies may also be able to provide important additional information if it is possible to determine MF exposures with reasonable accuracy and follow-up AD status on a sufficient number of participants.

Case-control studies of melatonin as a risk factor for AD and breast cancer are hampered by the fact that biological sequelae of both AD and breast cancer result in a decline of melatonin production to an unknown extent. (In breast cancer patients, there is a melatonin production rebound when tumors are surgically removed. In AD patients, the production of serotonin, the precursor of melatonin, is decreased and noradrenergic regulation becomes dysfunctional [78].) However, melatonin production is partially under genetic control. We have conducted a study of relatively healthy members of nuclear families and melatonin production (DOD Congressionally Directed Medical Research Program Grant: DAMD17-00-1-0692). The production of melatonin of the mother was successfully modelled as a function of the melatonin of a daughter, after adjusting for both the daughter's age and the influence of the father. This work allows for the design of case-control studies of the influence of long-term MF exposure on both melatonin production and the risks of breast cancer and AD.

4.2. ELF and/or RF MF exposure mitigation

It is also vital to mitigate both the extent of MF exposure and the effects of such exposure. Mitigation means efforts to both locate and shield or move the sources of MF away from individuals and design equipment which produces lower levels of MF. Little effort has apparently been spent on design issues. There are simple things that can be done. For example, almost all AC/DC transformers emit about 75 mG ELF MF fields. The exception, in our experience, has been a few transformers for Apple laptops measured about 10 years ago. AC/DC transformers are now everywhere, specifically under and around office desks and in nearly every room in a residence, often near the heads of beds. Maximizing one's distance from a transformer is important, because the strength of the MF field drops off with the square or cube of the distance from the source.

Seamstress is a very common profession and being a seamstress is clearly a risk factor for AD and quite possibly for breast cancer also. Seamstresses experience higher ELF MF exposure than members of almost any other profession. Older industrial sewing machines are extremely common all over the world. They produce extremely strong MFs, but it is possible to design "covers" for the motor to interfere with these fields, much as "headphones" can mitigate sound waves. Newer computer driven home sewing machines produce MF because of the AC/DC transformer. These transformers are placed in the arm of the machine, which results in high MF exposure to the operator. Simply by connecting the transformer to the machine by an electrical cord about three or more feet from the operator would mitigate a significant percentage of the MF exposure.

4.3. Biological mechanisms/experimental medicine research

We argue that, to the extent possible, research should now be conducted in humans. We list the following research questions as important examples of studying the biological effects of ELF and/or RF MF exposure:

1. Generation of peripheral amyloid beta
   a. Determination of intracellular Ca^{2+} ion concentration changes as a consequence of ELF or RF MF exposure.
   b. Measurement of the amount of $A\beta_{1-42}$ and $A\beta_{1-40}$ produced by and secreted from cells.
      i. This could be done at least by measuring blood levels of amyloid before and after ELF and/or RF MF exposure.
      ii. Perhaps there are more sophisticated experimental designs.
   c. Determination of which cell types in fact produce more amyloid beta after or during ELF and/or RF MF exposure.
   d. Determination of the dose response relationship(s) between ELF and/or RF MF exposure and cellular amyloid beta production.
   e. Measurement of the accumulation of amyloid beta in the brain, perhaps using PET scans [79,80].
2. Decrease in melatonin production

   Note: it is known that the pineal gland, the primary source of melatonin, has a tendency to become calcified and, perhaps, this is the reason why generally there is a reduction of melatonin production during aging.
   a. Determination of the extent of intracellular calcium within the pineal gland as a result of acute ELF and/or RF MF exposure.
   b. Determination of the extent of calcification of the pineal gland as a result of varying levels of long-term ELF and/or RF MF exposure.

Acknowledgement

The authors would like to thank Dr. James Burch, Arnold School of Public Health, University of South Carolina, for his review of Section 12 in the Bioinitiative Report.

References

[1] Z. Davanipour, E. Sobel, Section 12: Magnetic Field Exposure: Melatonin Production; Alzheimer's Disease; Breast Cancer, in: C.F. Blackman, M. Blank, M. Kundi, C. Sage (Organizing Committee), BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. URL: http://www.bioinitiative.org/report/docs/section_12.pdf.

[2] BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. URL: http://www.bioinitiative.org/report/index.htm.

[3] E.S. Schernhammer, S.E. Hankinson, Urinary melatonin levels and breast cancer risk, J. Natl. Cancer Inst. 97 (2005) 1084–1087.

[4] E.S. Schernhammer, F. Berrino, V. Krogh, G. Secreto, A. Micheli, E. Venturelli, S. Sieri, C.T. Sempos, A. Cavalleri, H.J. Schünemann, S. Strano, P. Muti, Urinary 6-sulfatoxymelatonin levels and risk of breast cancer in postmenopausal women, J. Natl. Cancer Inst. 100 (2008) 898–905.

[5] E. Sobel, Z. Davanipour, Electromagnetic field exposure may cause increased production of amyloid beta and eventually lead to Alzheimer's disease, Neurology 47 (1996) 1594–1600.

[6] E. Sobel, Z. Davanipour, R. Sulkava, T. Erkinjuntti, J. Wikstrom, V.W. Henderson, G. Buckwalter, J.D. Bowman, P.J. Lee, Occupations with exposure to electromagnetic fields: a possible risk factor for Alzheimer's disease, Am. J. Epidemiol. 142 (1995) 515–524.

[7] E. Sobel, M. Dunn, Z. Davanipour, Z. Qian, H.C. Chui, Elevated risk of Alzheimer's disease among workers with likely electromagnetic field exposure, Neurology 47 (1996) 1477–1481.

[8] Z. Davanipour, C.-C. Tseng, P.-J. Lee, E. Sobel, A case-control study of occupational magnetic field exposure and Alzheimer's disease: results from the California Alzheimer's Disease Diagnosis and Treatment Centers, BMC Neurol. 7 (2007) 13, http://www.biomedcentral.com/1471-2377/7/13.

[9] R. Mayeux, W.X. Tang, D.M. Jacobs, J. Manly, K. Bell, C. Merchant, S.A. Small, Y. Stern, H.M. Wisniewski, P.D. Mehta, Plasma amyloid beta-peptide 1–42 and incipient Alzheimer's disease, Ann. Neurol. 46 (1999) 412–416.

[10] R. Mayeux, L.S. Honig, M.X. Tang, J. Manly, Y. Stern, N. Schupf, P.D. Mehta, Plasma A[beta]40 and A[beta]42 and Alzheimer's disease: relation to age, mortality, and risk, Neurology 61 (2003) 1185–1190.

[11] C. Noonan, J. Reif, J. Burch, T.Y. Ichinose, M.G. Yost, K. K. Magnusson, Relationship between amyloid β protein and melatonin metabolite in a study of electric utility workers, J. Occup. Environ. Med. 44 (2002) 769–775.

[12] G.J.M. Maestroni, Therapeutic potential of melatonin in immunodeficiency states, viral diseases, and cancer, in: G. Heuther, W. Kochen, T.J. Simat, H. Steinhart (Eds.), Tryptophan, Serotonin, and Melatonin: Basic Aspects and Applications, Kluwer Academic/Plenum Publishers, New York, 1999, pp. 217–226.

[13] R.J. Reiter, D.-X. Tan, W. Qi, L.C. Manchester, M. Karbownik, J.R. Calvo, Pharmacology and physiology of melatonin in the reduction of oxidative stress in vivo, Biol. Signals Recept. 9 (2000) 160–171.

[14] M.A. Pappolla, M. Sos, R.A. Omar, R.J. Bick, D.L. Hickson-Bick, R.J. Reiter, S. Efthimiopoulos, N.K. Robakis, Melatonin prevents death of neuroblastoma cells exposed to the Alzheimer amyloid peptide, J. Neurosci. 17 (1997) 1683–1690.

[15] M.A. Pappolla, Y.J. Chyan, B. Poeggeler, P. Bozner, J. Ghiso, S.P. LeDoux, G.L. Wilson, Alzheimer beta protein mediated oxidative damage of mitochondrial DNA: prevention by melatonin, J. Pineal Res. 27 (1999) 226–229.

[16] M.A. Pappolla, M.J. Simovich, T. Bryant-Thomas, Y.J. Chyan, B. Poeggeler, M. Dubocovich, R. Bick, G. Perry, F. Cruz-Sanchez, M.A. Smith, The neuroprotective activities of melatonin against the Alzheimer beta-protein are not mediated by melatonin membrane receptors, J. Pineal Res. 32 (2002) 135–142.

[17] Y.X. Shen, W. Wei, S.Y. Xu, Protective effects of melatonin on cortico-hippocampal neurotoxicity induced by amyloid beta-peptide 25–35, Acta Pharmacol. Sin. 23 (2002) 71–76.

[18] P. Zatta, G. Tognon, P. Carampin, Melatonin prevents free radical formation due to the interaction between beta-amyloid peptides and metal ions [Al(III), Zn(II), Cu(II), Mn(II), Fe(II)], J. Pineal Res. 35 (2003) 98–103.

[19] M.H. Jang, S.B. Jung, M.H. Lee, C.J. Kim, Y.T. Oh, I. Kang, J. Kim, E.H. Kim, Melatonin attenuates amyloid beta25–35-induced apoptosis in mouse microglial BV2 cells, Neurosci. Lett. 380 (2005) 26–31.

[20] M. Pappolla, P. Bozner, C. Soto, H. Shao, N.K. Robakis, M. Zagorski, B. Frangione, J. Ghiso, Inhibition of Alzheimer beta-fibrillogenesis by melatonin, J. Biol. Chem. 273 (1998) 7185–7188.

[21] B. Poeggeler, L. Miravalle, M.G. Zagorski, T. Wisniewski, Y.J. Chyan, Y. Zhang, H. Shao, T. Bryant-Thomas, R. Vidal, B. Frangione, J. Ghiso, M.A. Pappolla, Melatonin reverses the profibrillogenic activity of apolipoprotein E4 on the Alzheimer amyloid Aβ peptide, Biochemistry 40 (2001) 14995–15001.

[22] Z. Skribanek, L. Balaspiri, M. Mak, Interaction between synthetic amyloid-beta-peptide (1–40) and its aggregation inhibitors studied by electrospray ionization mass spectrometry, J. Mass Spectrom. 36 (2001) 1226–1229.

[23] E. Matsubara, T. Bryant-Thomas, J. Pacheco Quinto, T.L. Henry, B. Poeggeler, D. Herbert, F. Cruz-Sanchez, Y.J. Chyan, M.A. Smith, G. Perry, M. Shoji, K. Abe, A. Leone, I. Grundke-Ikbal, G.L. Wilson, J. Ghiso, C. Williams, L.M. Refolo, M.A. Pappolla, D.G. Chain, E. Neria, Melatonin increases survival and inhibits oxidative and amyloid pathology in a transgenic model of Alzheimer's disease, J. Neurochem. 85 (2003) 1101–1108 (Erratum in: J. Neurochem. 86 (2003) 1312).

[24] Z. Feng, Y. Chang, Y. Cheng, B.L. Zhang, Z.W. Qu, C. Qin, J.T. Zhang, Melatonin alleviates behavioral deficits associated with apoptosis and cholinergic system dysfunction in the APP 695 transgenic mouse model of Alzheimer's disease, J. Pineal Res. 37 (2004) 129–136.

[25] X. Cheng, R.B. van Breemen, Mass spectrometry-based screening for inhibitors of β-amyloid protein aggregation, Anal. Chem. 77 (2005) 7012–7015.

[26] K.L. Clapp-Lilly, M.A. Smith, G. Perry, P.L. Harris, X. Zhu, L.K. Duffy, Melatonin acts as antioxidant and pro-oxidant in an organotypic slice culture model of Alzheimer's disease, Neuroreport 12 (2001) 1277–1280.

[27] Z. Feng, C. Qin, Y. Chang, J.T. Zhang, Early melatonin supplementation alleviates oxidative stress in a transgenic mouse model of Alzheimer's disease, Free Radic. Biol. Med. 40 (2006) 101–109.

[28] J. Quinn, D. Kulhanek, J. Nowlin, R. Jones, D. Pratico, J. Rokach, R. Stackman, Chronic melatonin therapy fails to alter amyloid burden or oxidative damage in old Tg2576 mice: implications for clinical trials, Brain Res. 1037 (2005) 209–213.

[29] K.L. Clapp-Lilly, M.A. Smith, G. Perry, L.K. Duffy, Melatonin reduces interleukin secretion in amyloid-beta stressed mouse brain slices, Chem. Biol. Interact. 134 (2001) 101–107.

[30] Y.X. Shen, S.Y. Xu, W. Wei, X.X. Sun, L.H. Liu, J. Yang, C. Dong, The protective effects of melatonin from oxidative damage induced by amyloid beta-peptide 25–35 in middle-aged rats, J. Pineal Res. 32 (2002) 85–89.

[31] S. Rosales-Corral, D.-X. Tan, R.J. Reiter, M. Valdivia-Velazquez, G. Martinez-Barboza, J.P. Acosta-Martinez, G.G. Ortiz, Orally administered melatonin reduces oxidative stress and proinflammatory cytokines induced by amyloid-beta peptide in rat brain: a comparative, in vivo study versus vitamin C and E, J. Pineal Res. 35 (2003) 80–84.

[32] D.K. Lahiri, D. Chen, Y.W. Ge, S.C. Bondy, E.H. Sharman, Dietary supplementation with melatonin reduces levels of amyloid beta-peptides in the murine cerebral cortex, J. Pineal Res. 36 (2004) 224–231.

[33] Y.X. Shen, W/Wei, J. Yang, C. Liu, C. Dong, S.Y. Xu, Improvement of melatonin to the learning and memory impairment induced by amyloid beta-peptide 25–35 in elder rats, Acta Pharmacol. Sin. 22 (2001) 797–803.

[34] M. Weinstock, S. Shoham, Rat models of dementia based on reductions in regional glucose metabolism, cerebral blood flow and cytochrome oxidase activity, J. Neural Transm. 111 (2004) 347–366.

[35] F. Tang, S. Nag, S.Y. Shiu, S.F. Pang, The effects of melatonin and Ginkgo biloba extract on memory loss and choline acetyltransferase activities in the brain of rats infused intracerebroventricularly with beta-amyloid 1–40, Life Sci. 71 (2002) 2625–2631.

[36] D.P. Cardinali, A.M. Furio, M.P. Reyes, Clinical perspectives for the use of melatonin as a chronobiotic and cytoprotective agent, Ann. NY Acad. Sci. 1057 (2005) 327–336.

[37] V. Srinivasan, S. Pandi-Perumal, D. Cardinali, B. Poeggeler, R. Hardeland, Melatonin in Alzheimer's disease and other neurodegenerative disorders, Behav. Brain Funct. 2 (2006) 15, doi:10.1186/1744-9081-2-15.

[38] Y. Cheng, Z. Feng, Q.Z. Zhang, J.T. Zhang, Beneficial effects of melatonin in experimental models of Alzheimer disease, Acta Pharmacol. Sin. 27 (2006) 129–139.

[39] J.Z. Wang, Z.F. Wang, Role of melatonin in Alzheimer-like neurodegeneration, Acta Pharmacol. Sin. 27 (2006) 41–49.

[40] Y.H. Wu, D.F. Swaab, The human pineal gland and melatonin in aging and Alzheimer's disease, J. Pineal Res. 38 (2005) 145–152.

[41] D.-X. Tan, L.C. Manchester, M.P. Terron, L.J. Flores, R.J. Reiter, One molecule, many derivatives: a never-ending interaction of melatonin with reactive oxygen and nitrogen species? J. Pineal Res. 42 (2007) 28–42.

[42] F. Peyrot, C. Ducrocq, Potential role of tryptophan derivatives in stress responses characterized by the generation of reactive oxygen and nitrogen species, J. Pineal Res. 45 (2008) 235–246.

[43] D.-X. Tan, L.C. Manchester, R.J. Reiter, W.B. Qi, M. Karbownik, J.R. Calvo, Significance of melatonin in antioxidative defense system: reactions and products, Biol. Signals Recept. 9 (2000) 137–159.

[44] R.J. Reiter, D.-X. Tan, S. Burkhardt, Reactive oxygen and nitrogen species and cellular and organismal decline: amelioration with melatonin, Mech. Ageing Dev. 123 (2002) 1007–1019.

[45] D.-X. Tan, L.D. Chen, B. Poeggeler, L.C. Manchester, R.J. Reiter, Melatonin: a potent, endogenous hydroxyl radical scavenger, Endocr. J. 1 (1993) 57–60.

[46] H.J. Bromme, W. Morke, D. Peschke, H. Ebelt, D. Peschke, Scavenging effect of melatonin on hydroxyl radicals generated by alloxan, J. Pineal Res. 29 (2000) 201–208.

[47] R.J. Reiter, L. Tang, J.J. Garcia, A. Munoz-Hoyos, Pharmacological actions of melatonin in oxygen radical pathophysiology, Life Sci. 60 (1997) 2255–2271.

[48] R.J. Reiter, D.-X. Tan, L.C. Manchester, W. Qi, Biochemical reactivity of melatonin with reactive oxygen and nitrogen species: a review of the evidence, Cell Biochem. Biophys. 34 (2001) 237–256.

[49] R.J. Reiter, D. Acuna-Castroviejo, D.-X. Tan, S. Burkhardt, Free radical-mediated molecular damage: mechanisms for the protective actions of melatonin in the central nervous system, Ann. NY Acad. Sci. 939 (2001) 200–215.

[50] I. Antolin, B. Obst, S. Burkhardt, R. Hardeland, Antioxidative protection in a high-melatonin organism: The dinoflagellate *Gonyaulax polydera* is rescued from lethal oxidative stress by strongly elevated, but physiologically possible, concentrations of melatonin, J. Pineal Res. 23 (1997) 182–190.

[51] M. Kotler, C. Rodriguez, R.M. Sainz, I. Antolin, A. Menendez-Pelaez, Melatonin increases gene expression for antioxidant enzymes in rat brain cortex, J. Pineal Res. 24 (1998) 83–89.

[52] M.I. Pablos, J.I. Chuang, J.R. Reiter, G.G. Ortiz, W.M. Daniels, E. Sewerynek, D. Melchiorri, B. Poeggeler, Time course of melatonin-induced increase in glutathione peroxidase activity in chick tissues, Biol. Signals 4 (1995) 325–330.

[53] L.R. Barlow-Walden, R.J. Reiter, A. Abe, M. Pablos, A. Menendez-Pelaez, L.D. Chen, B. Poeggeler, Melatonin stimulated brain glutathione peroxidase activity, Neurochem. Int. 26 (1995) 497–502.

[54] P. Montilla, I. Tunez, M.C. Munoz, J.V. Soria, A. Lopez, Antioxidative effect of melatonin in rat brain oxidative stress induced by Adriamycin, Rev. Esp. Fisiol. 53 (1997) 301–305.

[55] Vijayalaxmi, R.J. Reiter, M.L. Meltz, Melatonin protects human blood lymphocytes from radiation-induced chromosome damage, Mutat. Res. 346 (1995) 23–31.

[56] Vijayalaxmi, R.J. Reiter, T.S. Herman, M.L. Meltz, Melatonin and radioprotection from genetic damage: DNA damage in human blood lymphocytes, Mutat. Res. 371 (1996) 221–228.

[57] Vijayalaxmi, R.J. Reiter, M.L. Meltz, T.S. Herman, Melatonin: possible mechanisms involved in its "radioprotective" effect, Mutat. Res. 404 (1998) 187–189.

[58] C. Pieri, M. Marra, F. Moroni, R. Recchioni, F. Marcheselli, Melatonin: a peroxyl radical scavenger more effective than vitamin E, Life Sci. 55 (1994) 271–276.

[59] L. Tamarkin, M. Cohen, D. Roselle, C. Reichert, M. Lippman, B. Chabner, Melatonin inhibition and pinealectomy enhancement of 7,12-dimethylbenz(a)anthracene-induced mammary tumors in the rat, Cancer Res. 41 (1981) 4432–4436.

[60] P.N. Shah, M.C. Mhatre, L.S. Kothari, Effect of melatonin on mammary carcinogenesis in intact and pinealectomized rates in varying photoperiods, Cancer Res. 44 (1984) 3403–3407.

[61] L.S. Kothari, P.N. Shah, M.C. Mhatre, Pineal ablation in varying photoperiods and the incidence of 9,10-dimethyl-1,2-benzathracene induced mammary cancer in rats, Cancer Lett. 22 (1984) 99–102.

[62] A. Subramanian, L. Kothari, Suppressive effect by melatonin on different phases of 9,10-dimethyl-1,2-benzanthracene (DMBA)-induced rat mammary gland carcinogenesis, Anticancer Drugs 2 (1991) 297–303.

[63] A. Subramanian, L. Kothari, Melatonin, a suppressor of spontaneous murine mammary tumors, J. Pineal Res. 10 (1991) 136–140.

[64] D.-X. Tan, B. Poeggeler, R.J. Reiter, L.D. Chen, S. Chen, L.C. Manchester, L.R. Barlow-Walden, The pineal hormone melatonin inhibits DNA-adduct formation induced by the chemical carcinogen safrole in vivo, Cancer Lett. 70 (1993) 65–71.

[65] D.-X. Tan, R.J. Reiter, L.D. Chen, B. Poeggeler, L.C. Manchester, L.R. Barlow-Walden, Both physiological and pharmacological levels of melatonin reduce DNA adduct formation induced by the carcinogen safrole, Carcinogenesis 15 (1994) 215–218.

[66] S.R. Teplitzky, T.L. Kiefer, Q. Cheng, P.D. Dwivedi, K. Moroz, L. Myers, M.B. Anderson, A. Collins, J. Dai, L. Yuan, L.L. Spriggs, D.E. Blask, S.M. Hill, Chemoprevention of NMU-induced rat mammary carcinoma with the combination of melatonin and 9-cis-retinoic acid, Cancer Lett. 26 (2001) 155–163.

[67] K. Eck-Enriquez, T.L. Kiefer, L.L. Spriggs, S.M. Hill, Pathways through which a regimen of melatonin and retinoic acid induces apoptosis in MCF-7 human breast cancer cells, Breast Cancer Res. Treat. 61 (2000) 229–239.

[68] M. Karbownik, R.J. Reiter, J. Cabrera, J.J. Garcia, Comparison of the protective effect of melatonin with other antioxidants in the hamster kidney model of estradiol-induced DNA damage, Mutat. Res. 474 (2001) 87–92.

[69] R.T. Blickenstaff, S.M. Brandstadter, S. Reddy, R. Witt, Potential radioprotective agents. 1. Homologues of melatonin, J. Pharm. Sci. 83 (1994) 216–218.

[70] Vijayalaxmi, M.L. Meltz, R.J. Reiter, T.S. Herman, K.S. Kumar, Melatonin and protection from whole-body irradiation: survival studies in mice, Mutat Res. 425 (1999) 21–27.

[71] M. Karbownik, R.J. Reiter, W. Qi, J.J. Garcia, D.X. Tan, L.C. Manchester, Vijayalaxmi, Protective effects of melatonin against oxidation of guanine bases in DNA and decreased microsomal membrane fluidity in rat liver induced by whole body ionizing radiation, Mol. Cell. Biochem. 211 (2000) 137–144.

[72] R.J. Reiter, Pineal melatonin: cell biology of its synthesis and of its physiological interactions, Endocr. Rev. 12 (1991) 151–158.

[73] D.-X. Tan, L.C. Manchester, R.J. Reiter, W.B. Qi, M. Karbownik, J.R. Calvo, Significance of melatonin in antioxidant defense system: reactions and products, Biol. Signals Recept. 9 (2000) 137–159.

[74] R. Hardeland, I. Blazer, B. Poeggeler, B. Fuhrberg, H. Uria, G. Behrmann, R. Wolf, T.J. Meyer, R.J. Reiter, On the primary functions of melatonin in evolution: Mediation of photoperiodic signals in a unicell, photooxidation and scavenging of free radicals, J. Pineal Res. 18 (1995) 104–111.

[75] P. Stasica, P. Ulanski, J.M. Rosiak, Melatonin as a hydroxyl radical scavenger, J. Radioanal. Nucl. Chem. 232 (1998) 107–113.

[76] B. Halliwell, J.M. Gutteridge, Oxygen free radicals and iron in relation to biology and medicine: some problems and concepts, Arch. Biochem. Biophys. 246 (1986) 501–514.

[77] D.-X. Tan, L.C. Manchester, R.J. Reiter, B.F. Plummer, Cyclic 3-hydroxymelatonin: a melatonin metabolite generated as a result of hydroxyl radical scavenging, Biol. Signals Recept. 8 (1999) 70–74.

[78] Y.H. Wu, W.G. Feenstra, J.N. Zhou, R.Y. Liu, J.S. Toranõ, H.J. Van Kan, D.F. Fischer, R. Ravid, D.F. Swaab, Molecular changes underlying reduced pineal melatonin levels in Alzheimer disease: alterations in preclinical and clinical stages, J. Clin. Endocrinol. Metab. 88 (2003) 5898–5906.

[79] W.E. Klunk, H. Engler, A. Nordberg, Y. Wang, G. Blomqvist, D.P. Holt, M. Bergstrom, I. Savitcheva, G.F. Huang, S. Estrada, B. Ausen, M.L. Debnath, J. Barletta, J.C. Price, J. Sandell, B.J. Lopresti, A. Wall, P. Koivisto, G. Antoni, C.A. Mathis, B. Langstrom, Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B, Ann. Neurol. 55 (2004) 306–319.

[80] G.W. Small, V. Kepe, L.M. Ercoli, P. Siddarth, S.Y. Bookheimer, K.J. Miller, H. Lavretsky, A.C. Burggren, G.M. Cole, H.V. Vinters, P.M. Thompson, S.C. Huang, N. Satyamurthy, M.E. Phelps, J.R. Barrio, PET of brain amyloid and tau in mild cognitive impairment, N. Engl. J. Med. 355 (2006) 2652–2663.

ELSEVIER

Pathophysiology 16 (2009) 157–177

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Disturbance of the immune system by electromagnetic fields—A potentially underlying cause for cellular damage and tissue repair reduction which could lead to disease and impairment

Olle Johansson *

The Experimental Dermatology Unit, Department of Neuroscience, Karolinska Institute, Stockholm, Sweden

Received 23 August 2008; accepted 30 January 2009

Abstract

A number of papers dealing with the effects of modern, man-made electromagnetic fields (EMFs) on the immune system are summarized in the present review. EMFs disturb immune function through stimulation of various allergic and inflammatory responses, as well as effects on tissue repair processes. Such disturbances increase the risks for various diseases, including cancer. These and the EMF effects on other biological processes (e.g. DNA damage, neurological effects, etc.) are now widely reported to occur at exposure levels significantly below most current national and international safety limits. Obviously, biologically based exposure standards are needed to prevent disruption of normal body processes and potential adverse health effects of chronic exposure.

Based on this review, as well as the reviews in the recent Bioinitiative Report [http://www.bioinitiative.org/] [C.F. Blackman, M. Blank, M. Kundi, C. Sage, D.O. Carpenter, Z. Davanipour, D. Gee, L. Hardell, O. Johansson, H. Lai, K.H. Mild, A. Sage, E.L. Sobel, Z. Xu, G. Chen, The Bioinitiative Report—A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007)], it must be concluded that the existing public safety limits are inadequate to protect public health, and that new public safety limits, as well as limits on further deployment of untested technologies, are warranted.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Immunology; Radiofrequency fields; Magnetic fields; Power-frequency

1. Introduction

Around the world, for a number of years, there has been an active debate involving the general public, scientists, journalists, politicians, and people from the electric power and telecom companies, all trying to answer the basic question: Is biology compatible with the ever-increasing levels of electromagnetic fields (EMFs)? Or, to put it in more layman's terms: Can we, as human beings, survive all the radiation? Are we built for a 24-h, whole-body irradiation life? Are we immune to these signals, or are we actually playing with our planet's future, putting life at stake? The answers appear to be: *No, we are not designed for such EMF exposure loads. We are not immune. We are gambling with our future.*

Very often the biggest threat from EMF exposure is said to be cancer. However, this is not the most horrifying scenario. Just imagine if some basic *and general* molecular and/or cellular mechanism were altered. For instance, imagine if one morning the nitrogen-binding bacteria in the soil or the honey bees in the air had been destroyed beyond repair. Or, as this paper will indicate, imagine if our immune system, trying to cope with the ever-increasing electromagnetic signals, finally could not do so any longer!

Is the immune system designed to deal with "allergens" never present before, but now being invented, manufactured and used? Is it likely that our immune system, by some enormously intelligent 'glitch' in the evolutionary process has that capacity? Is that even remotely likely? *Of course, not.*

The recommended safe exposure levels have not taken this into account, since the existing standards are only based on the immediate heating of cells and tissues [most often evaluated in fluid-filled plastic dolls!]. They certainly do not take into consideration long-term effects or non-thermal effects that occur before heating can be detected. Furthermore, the recommendations do not take into account all available sci-

* Tel.: +46 8 52487073; fax: +46 8 303904.
E-mail address: olle.johansson@ki.se.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.03.004

entific reports. *The recommended exposure levels are not in any sense safe levels and are entirely inadequate.*

2. 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 outside world. These borders must be guarded, protected and constantly repaired since any damage to them could be fatal. In addition to these major borders there are number of other organ/tissue interfaces at which cellular conduct is monitored, evaluated and dealt with 24 h around the clock. Damage that is not detected and properly repaired in time can develop into cancer; something well known for ultraviolet light overexposure.

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 begin to multiply rapidly in the warm, moist, nutrient-rich environment. The cut may not be as 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 [2]. Such a leakage could indeed be fatal, causing nerve cell damage and followed by cellular death [3].

One of the first cell types encountered by a foreign organism after a cut in the skin is the phagocytic white blood cell. These cells congregate within minutes and begin to attack the invading foreign microbes. 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-recognizing 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 materials – 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. (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 when needed, 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 its production of pathogen-recognition molecules during the response.

A particularly interesting set of cells are the various dendritic cells of the skin as well as elsewhere. In the outermost cutaneous 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 [4] 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 household TVs and computer screens [5] 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. This indicates a direct EMF effect on skin and thyroid vasculature [[6–8]; for further details and refs., see below]. In the gastrointestinal tract, you will find corresponding types of cells guarding our interior lining against the outside world.

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, as you will

see, of utmost importance when we discuss the impact of the new electromagnetic fields of today's world.

For environmental substances to trigger hypersensitivity reactions, they must be fairly small in order to gain access to the immune system. Dust triggers a range of responses because the particles are able to enter the lower extremities of the respiratory tract, an area that is rich in adaptive immune-response cells. These dust particles can mimic parasites and may stimulate an antibody response. If the dominant antibody is IgE, the particles may subsequently trigger immediate hypersensitivity, which is manifest as allergies, such as asthma or rhinitis. If the dust stimulates IgG antibodies, it may trigger a different kind of hypersensitivity, e.g. farmer's lung [9].

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 [9].

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, electromagnetic fields could be said to fulfil the most important demand: they penetrate the entire body.

The hypersensitivity classification system was first described by Coombs and Gell [cf. ref. 10]. The system classifies the different types of hypersensitivity reaction by the types of immune responses involved. 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 has its respective role in clearing infections.

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 its known enemies. *Among the known enemies one will not find modern electromagnetic fields, such as power-frequency electric and magnetic fields, radiowaves, TV signals, mobile phone or WiFi microwaves, radar signals, X-rays or artificial 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 defences. They penetrate the body, and some have already proven to be fatal. 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). In retrospect, that was just plain madness. However, the persons doing so and selling these gadgets were not misinformed or less intelligent. The knowledge at the time was deficient, as was a competent risk analysis coupled to a parallel analysis of public needs.

3. Electromagnetic fields – now and previously

The electromagnetic spectrum 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, radioactivity and cosmic rays. Electromagnetic fields are present everywhere in our environment, and except for the visible spectrum, they are invisible to the human eye.

An electromagnetic field consists 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. Magnetic fields as low as around 0.2 μT (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 [11,12], 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.

Even the extremely low frequencies (ELF) that are widely used in powerlines and domestic appliances should be viewed with caution. In June 2007, the World Health Organization (WHO) pointed out that 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. At radiofrequencies, electric and magnetic fields are closely interrelated and we typically measure their levels as power densities in Watts per square metre (W/m^2).

4. Electromagnetic fields and health

Life on Earth, since its beginning more than 3.5 billion years ago, has developed under the influence of the practically static geomagnetic field and the radiation from the sun. All living organisms that have not been able to directly cope with these influences are either gone or have adapted in one of several ways. Living under-ground, only being active during night, living in the deeper waters (at least from 1 m and down

below) of our oceans and lakes, under the foliage of the jungle trees, or having developed a skin (or, for plants, a cortex) containing a pigment (animals and plants have very similar ones) that will shield from some heat and some sunshine. Any fair-skinned Irish or Scandinavian person learns very early to avoid even the bleak sun up-north to avoid a nasty sunburn. That sunburn will develop into a postinflammatory hyperpigmentation, that may have cosmetic value, but will also cause a redness of the skin as well as heat and pain/itch sensations.

But, during the last 100 years we have found that the pigment in our skin does not furnish any protection against other frequencies. Cosmic rays, radioactivity, X-rays, UVC, UVB and now even UVA are considered, together with radar-type microwaves to be very dangerous to health. We are translucent to power–frequency magnetic fields as well as mobile phone and WiFi microwaves, but this does not mean that they are without possible effects, through thermal or non-thermal mechanisms.

For me, as a scientist, this poses the main relevant questions: Is it possible to adapt our biology to altered exposure conditions in less than 100 years, or do we have to have thousands of years – or longer – for such an adaptation? And, in the meantime, what kind of safety standards must we adopt? A 'prudent avoidance' strategy, ALARA, recommendation levels based only on thermal effects, or is the only actual safe safety level for such exposures 0 (zero) Watts/kg until we really know? Or is "human progress", profit and greed more important than possible damage to our health? How far can we push the Russian roulette? And who should decide about this? Who should be held responsible if something goes wrong?

Our limited understanding of the biological effects of the vast majority of frequencies gives reason for concern. Although there is still a debate in this regard, *tinnitus, brain tumours and acoustic neuroma clearly are associated with cell phones and mobile phones, as is childhood leukemia with powerlines* (for references, see Blackman et al. [1]).

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 many orders of magnitude higher than natural background levels. The same is true for appliances using power frequencies.

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

It is worth noting that 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 powerlines), ELF-modulated radiofrequency fields, continuous wave radiofrequency radiation and particularly pulsed radiofrequency signals are more or less bioactive, e.g. as neurotoxic, immune-disrupting and/or carcinogenic environmental exposure parameters. As will be discussed below, hazardous effects on the immune system of this potential environmental toxin must be seriously considered.

5. Effects of electromagnetic fields on the immune system

An ever-increasing number of studies has clearly shown various biological and medical effects at the cellular level due to electromagnetic fields, including power–frequency, radiofrequency and microwaves. Such fields are present in everyday life, at the workplace, in homes and places of leisure.

5.1. The functional impairment electrohypersensitivity (EHS)

One of the first observations of a direct effect on the immune system was the finding in the 1980s of persons with the functional impairment electrohypersensitivity (EHS), namely those who claim to suffer from 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, WiFi equipments, as well as other electromagnetic devices. Frequently, symptoms from internal organ systems, such as the heart and the central nervous system, are also encountered [13].

Persons with EHS experience facial skin symptoms (sensory sensations of the facial skin including stinging, itching, burning, erythema, rosacea), eye irritation, runny or stuffy nose, impaired sense of smell, hoarse dry throat, coughing, sense of pressure in ear(s), tinnitus, fatigue, headache, "heaviness" in the head, sleeplessness, nausea/dizziness, cardiac symptoms and difficulties in concentrating. In the Cox [14] report on electrical hypersensitivity in the United Kingdom, mobile phone users' symptoms 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 persons with symptoms from cell phone masts was 18%, DECT cordless phones (36%), landline phones (6%), VDTs (27%), television (12%) and fluorescent lights (18%). In addition, Fox [15] reported that a questionnaire survey of EHS individuals revealed symptoms of nausea, and of dizziness/disorientation.

Levallois et al. [16] in 2002 reported on their study of prevalence of self-perceived hypersensitivity to EMF in California. They found that about 3% of the population reports to be electrohypersensitive. About 0.5% of the population reported the necessity to change jobs or remain unemployed due to the severity of their 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 engage in 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 North America. The results were based on a telephone survey among a sample of 2072 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 disability in North America.

A recent German survey [17] suggests that the prevalence of subjects who attribute health complaints to EMF exposures is not negligible. In a sample of 2500 interviewees, 8% specifically attributed health complaints to exposures from mobile phone base station antennas or the use of mobile or cordless phones. 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, the European Group of Experts reported that electrical hypersensitivity had a higher prevalence in Sweden, Germany, and Denmark than in the United Kingdom, Austria, and France. All these data suggest that the true number is still uncertain and requires further research (cf. Schüz et al. [18]).

Roosli et al. [19,20] estimate that the proportion of individuals in Switzerland with EHS symptoms is about 5%, where the exposures of concern are cited to be mobile phone base stations (74%), followed by mobile phones (36%), cordless phones (29%), and powerlines (27%). They reported that about half the Swiss population is concerned about health effects from EMF exposures in general.

The WHO has acknowledged the condition of electrohypersensitivity, and published in 2006 a research agenda for radiofrequency fields. 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.

Lyskov et al. [21] in 2004 reported that EHS individuals exhibited sensitivity to VDTs, fluorescent lights and television, all of which produce flickering light. EHS individuals who 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. In 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. [N.B. It may just show that they feel ill. It is very hard for me to understand how sensitivity to flickering light could account for EHS in conjunction with e.g. mobile phones and base stations.]

Mueller and Schierz [22], also in 2004, reported that soundness of sleep and well-being in the morning, but not sleep quality, were affected by overnight EMF exposure in EHS individuals. 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, something which may have strong implications for disease development (cf. Hallberg and Johansson, submitted).

Markovà et al. [23] reported that non-thermal microwave exposure from global system for mobile communication (GSM) mobile telephones at lower levels than the International Commission for Non-Ionizing Radiation Protection (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 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 tumour suppressor p53-binding protein 1 (53BP1) and phosphorylated histone H2AX (γ-H2AX), which have been shown to co-localize 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. *N.B. These effects occurred at non-*

thermal microwave exposure levels from mobile telephones that are permissible under safety standards of ICNIRP!

The same group after having described frequency-dependent effects of mobile phone microwaves (MWs) of GSM on human lymphocytes from EHS persons and healthy persons (see above), went ahead asking themselves this: Contrary to GSM, universal global telecommunications system (UMTS) mobile phones emit wide-band MW signals. Hypothetically, UMTS MWs may result in higher biological effects compared to GSM signals because of eventual "effective" frequencies within the wideband. Based on this hypothesis they have very recently reported for the first time that UMTS MWs affect chromatin and inhibit formation of DNA double-strand breaks co-localizing 53BP1/γ-H2AX DNA repair foci in human lymphocytes from hypersensitive and healthy persons and confirm that effects of GSM MWs depend on carrier frequency [24]. Remarkably, the effects of MWs on 53BP1/γ-H2AX foci persisted up to 72 h following exposure of cells, even longer than the stress response following heat shock. The data are in line with the hypothesis that the type of signal, UMTS MWs, may have higher biological efficiency and possibly larger health risk effects compared to GSM emissions. No significant differences in effects between groups of healthy and hypersensitive subjects were observed, except for the effects of UMTS MWs and GSM – 915 MHz MWs on the formation of the DNA repair foci, which were different for hypersensitive ($p < 0.02$[53BP1]//0.01[γ-H2AX]) but not for control subjects ($p > 0.05$). The non-parametric statistics used here did not indicate specificity of the differences revealed between the effects of GSM and UMTS MWs on cells from hypersensitive subjects and more data are therefore needed to study the nature of these differences.

5.2. *EHS as radiation damage/the mast cell hypothesis*

Persons claiming adverse skin reactions after having been exposed to computer screens or mobile phones 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 you would do if you had been exposed to e.g. sun rays, X-rays, radioactivity or chemicals. My working hypothesis, thus, 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 [25,26]. This is also covered in great depth by the author Gunni Nordström in her latest book [27].

Very early, immune cell alterations were observed when exposing two EHS individuals to a TV monitor [4]. In this article, we used an open-field provocation, in front of an ordinary TV set, of persons regarding themselves as suffering from skin problems due to work at video display terminals. Employing immunohistochemistry, in combination with a wide range of antisera directed towards cellular and neurochemical markers, we were able to show 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. This latter finding may be due to 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 [28]. 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 had 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 showing mast cell epidermiotrophism. 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 were demonstrated later on in an experimental situation employing normal healthy volunteers in front of visual display units, including ordinary television sets [5].

Mast cells, when activated, release a wide range 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 cited studies, it is clear that electromagnetic fields affect the mast cell and 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 common symptoms reported from persons suffering from EHS/screen dermatitis. Mast cells occur in the brain [29] and their presence may, under the influence of EMF and/or radiofrequency radiation exposure lead to a 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 EMF with cardiac function have demonstrated that changes are present in the heart after exposure. Some electrically sensitive people have symptoms similar to heart attacks or strong heart palpitations after exposure to EMF.

We have also, in more detail, compared facial skin from EHS persons with corresponding material from normal healthy volunteers [30]. 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), 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 ongoing investigations, we have also found alterations of the Merkel cell number in the facial skin of electrohypersensitive persons (Yoshimura et al., in preparation). However, it has to be pointed out that we cannot draw any definitive conclusions about the cause of the changes observed, based upon those results. Blind or double-blind provocations in a controlled environment [5] are necessary to elucidate the underlying causes for the changes reported in this particular investigation. So far, unfortunately, I and my co-workers have not been able to attract funding for such studies.

Gangi and Johansson [31,32] have proposed models for how mast cells and substances secreted from them (e.g., histamine, heparin, and serotonin) could explain sensitivity to EMF similar to those used to explain UV- and ionizing radiation-related damages. We discuss the 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 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 EHS persons similar to those observed in the skin damaged due to UV light or ionizing radiation.

Dr. Shabnam Gangi and I, in two theoretical papers [31,32], have put forward a model for how mast cells and substances secreted from them could explain sensitivity to EMF. The model starts from known facts in the fields of UV- and ionizing radiation-related damages, and uses all the new studies dealing with alterations seen after e.g. power frequency or microwave EMF to propose a simple summarizing model for the phenomenon of electrohypersensitivity.

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.

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, nitric oxide (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 in EHS persons 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 also be addressed in controlled studies.

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.

Holmboe and Johansson [33] reported on testing EHS persons for increased levels of IgE or signs of a positive Phadiatop Combi (which is a screening test for allergies towards

certain foods, pollens, insects, and other animals) both of which would be indicators of an immune system alert. Five men and 17 women participated in the study. Skin and nervous system effects were the primary symptoms reported. 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 EHS persons had tinnitus. However, no connection between IgE blood levels and symptoms was found. All EHS people had normal values (<122 kU/l). Only three people had a positive Phadiatop Combi.

In summary, it is evident from our preliminary experimental data that various biological alterations are present in EHS persons claiming to suffer from exposure to EMF. The alterations are themselves enough to fully explain the EHS symptoms, and the involvement of the immune system is evident.

Thus, it is of paramount importance to continue investigating persons with EHS. We would favour studies of EMF 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 is very important. Finally, not to be forgotten, a general investigation of persons with EHS versus normal healthy volunteers regarding the above markers as well as other markers for cell traffic, proliferation and inflammation is very much needed. Such research may lay a firm foundation for necessary adjustment of accessibility, thus helping all persons with EHS.

5.3. Rat skin and thyroid: animal model studies

In addition to the studies in humans, we have also done a series of animal experiments [6–8]. These have been a collaborative effort between the Department of Biology, Faculty of Sciences, Novi Sad, Serbia, and my own research group at the Karolinska Institute, Stockholm, Sweden.

These papers go back to early observations in persons with EHS where large increases in the cutaneous mast cell count could be demonstrated as compared to normal healthy volunteers. A corresponding effect on cutaneous mast cells from normal healthy volunteers placed in front of ordinary TVs/PCs could also be shown. My working hypothesis since then is that EHS is a kind of radiation damage, since the observed cellular changes are very much the same as the ones you would find in tissue subjected to UV-light or ionizing radiation (for refs., see above).

One very fierce criticism has been that such mast cell alterations in persons with electrohypersensitivity (or in normal healthy volunteers!) can not be due to EMFs and/or airborn chemicals, but must be due to psychological or psychiatric personality disturbances, cognitive malfunction, or likewise.

The aim of these studies has therefore been 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–frequency (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, CGRP, and PGP 9.5 were applied to skin sections and PGP 9.5, 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, both the light microscope and the ultrastructural results show the stimulating effect of power–frequency EMFs.

The results obtained in animal studies cannot be understood by psychological or psychiatric theories, but are clearly related to the EMF exposure. In view of recent epidemiological studies, pointing to a correlation between long-term exposure from power-frequency magnetic fields or radio-/microwaves and cancer, our data have to be taken seriously.

5.4. Cutaneous heat shock protein/stress response pathway

Recent evidence by Leszczynski et al. has indicated activation of stress-induced pathways in cultivated cells in response to microwaves [34]. Their article indicated that mobile telephone microwaves activate a variety of cellular signal transduction pathways, among them the hsp27/p38MAPK stress response pathway [34]. 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 expres-

sion changes in human endothelial cell lines with microwave 900 MHz mobile phone exposure [35].

5.5. Childhood leukemia and power-frequency magnetic fields; CNS tumours and cell phone use

Childhood leukemia was connected to power-frequency magnetic fields already in the pioneering work by Wertheimer and Leeper [36]. More recently, Scandinavian scientists have identified an increased risk for acoustic neuroma (i.e., a benign tumour of the eighth cranial nerve) in cell phone users, as well as a slightly increased risk of malignant brain tumours such as astrocytoma and meningioma on the same side of the brain as the cell phone was held [37–40]. In addition, a clear association between adult cancers and FM radio broadcasting radiation has been noticed, both in time and location [41–43]. Initial studies on facial nevi indicate that nowadays young children can have a substantial number of these (Hallberg and Johansson, unpublished data). If, in addition to the low-frequency EMF, there is a radiofrequency and/or microwave correlation, then this must be considered in future research and safety programs.

5.6. Effects by microwaves on acute experimental allergic encephalomyelitis

Turning back to the immune system, Anane et al. [44] have 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 non-habituated 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.

5.7. Effects of electromagnetic fields on immune system parameters, including cellular markers

5.7.1. Residential exposure effects/occupational studies

The object of the study by Boscol et al. [45] in 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 radio–television 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 only be considered as very serious, since this could hamper the immune system in its daily struggle against various organisms/agents.]

A more general reaction pattern was found by Dmoch and Moszczynski [46] 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, a decreased count of NK cells and a lower value of T-helper/T-suppressor ratio were found.

The immunoglobulins' concentrations and T-lymphocyte subsets during occupational exposures to microwave radiation were also assessed in 1999 by Moszczynski et al. [47]. In the workers of re-transmission 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 behaviors of examined immunological parameters indicate that the effect of microwave radiation on the immune system depends on the exposure. However, disorders in the immunoglobulins' concentrations and in the T8 cell count had not, so far, caused any reported clinical consequences in their workers.

Tuschl et al. [48] 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, decimetre 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 with the above mentioned devices. Eighteen exposed and 13 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 quantifying subpopulations of immunocompetent cells, the activity of lymphocytes was measured. Lymphocytes were stimulated by mitogen phytohemagglutinin and their proliferation measured by flow cytometry. No statistically significant differences between the control and exposed persons were found. In both study groups all immune parameters were within normal ranges.

5.7.2. Electromagnetic fields and atopy

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. [49] 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 PBMC of atopic women (groups B and D) stimulated by 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 trans–trans 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 – possibly dependent on varying immune functions based on variations in genetic make-up. [This is of particular interest since EHS persons have certain atopic features (Liden, personal communication) that may make them more susceptible to EMFs.]

5.7.3. Animal and human cellular in vivo and in vitro studies

One very interesting set of experiments was performed by Cleary et al. [50] in 1990. Whole human blood was exposed or sham-exposed in vitro for 2 h to 27 or 2450 MHz radiofrequency (RF) radiation under isothermal conditions (i.e., 37 ± 0.2 °C). Immediately after exposure, mononuclear cells were separated from blood by Ficoll density-gradient centrifugation and cultured for 3 days at 37 °C with or without mitogenic stimulation by 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 indicate that the biphasic, dose-dependent effects of the radiation on lymphocyte proliferation are not dependent on heating.

Half a decade later (1996), Cleary et al. [51] published yet another paper with the title "Effect of isothermal radiofrequency radiation on cytolytic T lymphocytes". Previous in vitro studies had provided evidence that RF radiation modulates proliferation of human glioma, lymphocytes, and other cell types. The mechanism of such cell proliferation modulation, as well as mechanisms for effects on other cell physiologic endpoints, however, was 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 2450 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, 2450 MHz exposure increased CTLL-2 proliferation immediately after exposure but reduced 24 h postexposure proliferation. RF radiation effects depended on the mitotic state of the cells at the time of exposure.

In 1992, Czerska et al. [52] studied the effects of continuous and pulsed 2450-MHz radiation on spontaneous lymphoblastoid transformation of human lymphocytes in vitro. Normal human lymphocytes were isolated from the peripheral blood of healthy donors. One-milliliter 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) 2450-MHz radiation at non-heating (37 °C) and various heating levels (temperature increases of 0.5, 1.0, 1.5, and 2 °C). The pulsed exposures involved 1-μs pulses at pulse repetition frequencies from 100 to 1000 pulses/s 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 2450-MHz radiation acts differently on the process of lymphoblastoid transformation in vitro compared with CW 2450-MHz radiation at the same average SARs.

In 2003, Dabrowski et al. [53] exposed samples of mononuclear cells isolated from peripheral blood of healthy donors ($n = 16$) to 1300 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 $S = 10\,\mathrm{W/m^2}$ ($1\,\mathrm{mW/cm^2}$). 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 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 IFNg remained unchanged or slightly decreased in the culture supernatants. Concomitantly, the microwave irradiation modulated the monokine production by monocytes. The production of IL-1b increased significantly ($p < 0.01$), the concentration of its antagonist (IL-1ra) dropped by half ($p < 0.01$) and the tumour necrosis factor (TNF-α) concentration remained unchanged. These changes of monokine proportion (IL-1b versus IL-1ra) resulted in significant increase of the value of the LM (=the monokine influence on lymphocyte mitogenic response; cf. Dabrowski et al. [54]) 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_0 phase PBMC exposed to low-level (SAR = 0.18 W/kg) pulse-modulated 1300 MHz microwaves and subsequently cultured, demonstrating changed immune activity (as of above), in 2006 Stankiewicz et al. [55] 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 EMF. 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 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 a very important warning signal as well as a very important piece of the explanatory jigsaw puzzle regarding EHS. 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 too high an activation level?]

Two papers of paramount importance are Donnellan et al. [56] and Harvey and French [57]. In the first, a mast cell line, RBL-2H3, was exposed to 835 MHz for 20 min, three times per day for 7 days at a power density of $8.1 \pm 3\,\mathrm{mW/cm^2}$. From day 4 onwards, it was observed that the rate of DNA synthesis and cell replication increased, that actin distribution and cell morphology became altered, and that the amount of beta-hexosaminidase (a marker of granule secretion) released in response to a calcium ionophore was significantly enhanced, in comparison to unexposed cultures. No effects were seen on levels of cytoskeletal protein synthesis or of beta-actin mRNA. Morphological changes persisted following subculture for at least 7 days in the absence of further exposure. It is hypothesized that effects of exposure to an EMF at 835 MHz may be mediated via a signal transduction pathway. In the second publication, Harvey and French used a resonant cavity which delivered a continuous wave exposure at 864.3 MHz at an average SAR of 7 W/kg to determine non-thermal biological effects of microwave exposure. A human mast cell line, HMC-1, was used as the biological target. Cells were exposed three times for 20-min duration daily, for 7 days. The temperature of the cell culture medium during the exposure fell to 26.5 °C. Effects were seen on localization of protein kinase C, and expression of three of the 588 genes screened. The affected genes included the proto-oncogene c-kit, the transcription factor nucleoside diphosphate kinase B and the apoptosis-associated gene DAD-1. Stress response genes were variably upregulated. No significant effect on morphology or on F-actin distribution was detected. They concluded that low-power microwave exposure may act on HMC-1 cells by altering gene expression via a mechanism involving activation of protein kinase C, and at temperatures well below those known to induce a heat shock response.

Elekes et al. [58] in 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 μW/cm^2) in vivo increases the cytotoxic activity of natural killer cells of rat spleen [59]. 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 μW/cm^2 caused a significant enhancement of TNF production in peritoneal macrophages and splenic T-lymphocytes [60]. 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 cellular immunity!

A very intriguing investigation was carried out by Gapeev et al. [61], who compared horn, dielectric and channel antennae and their matching with various types of loads, including a biological object. The channel antenna in contrast to dielectric and horn provides the 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. It is shown, that low-intensity electromagnetic radiation of extremely high frequency in near field zone of the channel radiator modifies 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. No frequency dependence has been found 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. [62] 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 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 concluded 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. [63], 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/cm^2, 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 non-specific 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 normal 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 [64]. 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/cm^2

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 a series of five 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 single low-intensity extremely high-frequency electromagnetic radiation, at 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.

Experiments have also been conducted to elucidate the effects of chronic low power-level microwave radiation on the immunological systems of rabbits [65]. Fourteen male Belgian white rabbits were exposed to microwave radiation at 5 mW/cm^2, 2.1 GHz, 3 h daily, 6 days/week for 3 months in two batches of seven 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 was 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 ($p < 0.01$) and during follow-up ($p < 0.01$). The first batch of animals was 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 "better" response than the control group (delta % +12.4 versus +7.54).

Nasta et al. [66], 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 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. [66] 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 μW/cm^2 caused a significant enhancement of tumour necrosis factor production in peritoneal macrophages [67]. 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 μW/cm^2 on the tumour necrosis factor (TNF) production and immune response was tested by Novoselova et al. [68]. 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. A diet containing lipid-soluble nutrients (beta-carotene, alpha-tocopherol and ubiquinone Q9) increased the activity of macrophages and T-cells from irradiated mice. These results demonstrate that irradiation with low-power density microwaves stimulates the immune potential of macrophages and T-cells, and the antioxidant treatment enhances the effect of microwaves, in particular when the effect of irradiation is reduced.

In the experimental study by Çetin et al. [69] in 2006, the hematological effects of pulsed EMFs chronic exposure were investigated on mice. Sixty, 6-week-old male Swiss mice, weighing 40–45 g were used, and were divided into two groups: in one group, animals ($n = 30$) were exposed to pulsed EMFs (60 Hz, intensity 3 μT, 12 h by day) for a 120-day period, whereas the second group ($n = 30$) was used as control. On days 15, 30, 90 and 120, samples were taken by cardiac puncture for the hematological analysis (red blood cell and white blood cell counts, leukocyte distribution). Whereas no significant difference was noted between control and exposed animals at the 15th and the 30th days, a macrocytic anemia characterized by decreases in of hemoglobin concentration, hematocrit values and erythrocyte counts and by increases in mean corpuscular volume, occurred in the exposed animals on day 90. Furthermore, they have shown significant reductions of leukocyte, lymphocyte and neutrophil counts, while monocyte counts were increased. On day 120, these leukocyte alterations were still

observed, whereas erythrocyte parameters approached control values. These results suggest that pulsed electromagnetic fields (60 Hz and 3 μT) affect the hematological parameters of mice, probably by reducing proliferation and differentiation of marrow stem cells.

Obukhan [70] has performed cytologic investigations designed to study bone marrow, peripheral blood, spleen, and thymus of albino rats irradiated by an EMF of 2375, 2450, and 3000 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 were revealed. The results permitted establishing the probability-threshold levels of exposure taking account of reactions of perception and physiologic adaptation together with compensatory and regenerative processes and the injury sustained. It was shown that changes in bone marrow cells differentiation and reproduction, rather than integral shifts in the peripheral blood, acquired the utmost significance. The blast cell population increased in low-intensity exposure, along with disturbances in mitosis.

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 et al. [71]. The chosen SAR values are near the upper limit of energy absorbed by localized tissue during the use of 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 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 X-radiation. Within the experimental parameters of the study in all instances no effect from the RFR signal was observed. [Of course, DNA damage is a well characterized effect of electromagnetic irradiation of other cell types, including lymphoblastoid cells [72], fibroblasts [73], and brain cells [74].]

Despite the important role of the immune system in defending the body against infections and cancer, only rather few investigations on possible effects of RF radiation on function of human immune cells have been undertaken. One of these is the investigation by Tuschl et al. [75] in 2006 where they assessed whether GSM modulated RF fields have adverse effects on the functional competence of human immune cells. Within the frame of a multidisciplinary project "Biological effects of high frequency electromagnetic fields (EMFs)" 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 ΔT of 0.06 °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 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 tumour 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 was no indication that emissions from mobile phones are associated with adverse effects on the human immune system.

Chagnaud and Veyret [76] in 1999 could also 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.

[N.B. One must always be very cautious when it comes to negative findings. For example: of the 100 or so papers on genotoxic effects of RF fields, a majority has been done with peripheral blood lymphocytes. Except for special cases, these cells are highly protected from their upregulated repair enzymes. These cells are often used to investigate chemical genotoxicity, because in these cases the toxicity often occurs due to the action of the repair enzymes. Repair-deficient cells remain intact! The mechanisms of action of EMFs may not be clearly understood, but it is unlikely they mimick such chemical enzyme-induced genotoxicity. — Yet another example is the use of mice and rats for the study increases in brain tumour incidence due to mobile telephony exposure. Since the incidence data from human studies point to a needed exposure time of at least 5 years, and mice and rats do not live longer

than 2 years, the rats will die long before they have had a chance to develop the tumours!]

Irradiation by pulsed microwaves (9.4 GHz, 1 μs pulses at 1000/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 [77]. 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 $\mu W/cm^2$; whole-body averaged SAR approximately 0.015 W/kg). Sham exposure or microwave irradiation took place during each of 5 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.

To study the possible RF effects on human lymphocyte activation, Capri et al. [78] analyzed CD25, CD95, CD28 molecules in unstimulated and stimulated CD4+ or CD8+ T-cells in vitro. Peripheral blood mononuclear cells (PBMCs) from young and elderly donors were exposed or sham-exposed to RF (1800 MHz, SAR 2 W/kg) with or without mitogenic stimulation. No significant changes in the percentage of these cell subsets were found between exposed and sham-exposed lymphocytes in both young and elderly donors. Nevertheless, after RF exposure they observed a slight, but significant, downregulation of CD95 expression in stimulated CD4+ T-lymphocytes from elderly, but not from young donors. This age-related result is noteworthy given the importance of such a molecule in regulation of the immune response.

In the paper by Yurekli et al. [79], a GHz transverse electromagnetic (GTEM) cell was used as an exposure environment for plane wave conditions of far-field free space EMF propagation at the GSM base transceiver station (BTS) frequency of 945 MHz, and effects on oxidative stress in rats were investigated. When EMFs at a power density of 3.67 W/m^2 (SAR = 11.3 mW/kg), which is well below current exposure limits, were applied, MDA (malondialdehyde) level was found to increase and GSH (reduced glutathione) concentration was found to decrease significantly ($p < 0.0001$). Additionally, there was a less significant ($p = 0.019$) increase in SOD (superoxide dismutase) activity under EMF exposure.

Since genotoxic effects of the second generation standard GSM have been reported after exposure of human cells in vitro, Schwarz et al. [80] decided to use human cultured fibroblasts of three different donors and three different short-term human lymphocyte cultures and expose them to 1950 MHz UMTS below the SAR safety limit of 2 W/kg. The alkaline comet assay and the micronucleus assay were used to ascertain dose and time-dependent genotoxic effects. Five hundred cells per slide were visually evaluated in the comet assay and comet tail factor (CTF) was calculated. In the micronucleus assay 1000 binucleated cells were evaluated per assay. The origin of the micronuclei was determined by fluorescence labeled anticentromere antibodies. All evaluations were performed under blinded conditions. UMTS exposure increased the CTF and induced centromere-negative micronuclei (MN) in human cultured fibroblasts in a dose and time-dependent way. Incubation for 24 h at an SAR of 0.05 W/kg generated a statistically significant rise in both CTF and MN ($p = 0.02$). At an SAR of 0.1 W/kg the CTF was significantly increased after 8 h of incubation ($p = 0.02$), the number of MN after 12 h ($p = 0.02$). However, under these conditions, no UMTS effect was obtained with lymphocytes, either unstimulated or stimulated with phytohemagglutinin. The authors conclusion was that UMTS exposure may cause genetic alterations in some but not in all human cells in vitro.

Simkó and Mattsson [81] have presented a hypothesis of a possible initial cellular event affected by exposure to ELF-EMF, an event that is compatible with the multitude of effects observed after exposure. Based on an extensive literature review, they suggested that ELF-EMF exposure is able to perform such activation by means of increasing levels of free radicals. Such a general activation is compatible with the diverse nature of observed effects. Free radicals are intermediates in natural processes, like mitochondrial metabolism, and are also a key feature of phagocytosis. Free radical release is inducible by ionizing radiation or phorbol ester treatment, both leading to genomic instability. EMFs might be a stimulus to induce an "activated state" of the cell such as phagocytosis, which then enhances the release of free radicals, in turn leading to genotoxic events. Simkó and Mattsson envisaged that EMF exposure can cause both acute and chronic effects that are mediated by increased free radical levels: (1) Direct activation of, for example macrophages (or other cells) by short-term exposure to EMF leads to phagocytosis (or other cell-specific responses) and consequently, free radical production. This pathway may be utilized to positively influence certain aspects of the immune response, and could be useful for specific therapeutic applications. (2) EMF-induced macrophage (cell) activation includes direct stimulation of free radical production. (3) An increase in the lifetime of free radicals by EMF leads to persistently elevated free radical concentrations. In general, reactions in which radicals are involved become more frequent, increasing the possibility of DNA damage. (4) Long-term EMF exposure leads to a chronically increased level of free radicals, subsequently causing an inhibition of the pineal gland hormone melatonin. Taken together, these EMF-induced reactions could lead to a higher incidence of DNA damage and therefore, to an increased risk of tumour development. While the effects on melatonin and the extension of the lifetime of radicals can explain the link between EMF

exposure and the incidence of for example leukaemia, the two additional mechanisms described by them specifically for mouse macrophages, can explain the possible correlation between immune cell system stimulation and EMF exposure.

5.7.4. *Effects of EMFs on the immune system at pregnancy*

Nakamura et al. [82] have investigated a very important issue, namely what happens to pregnant rats exposed to microwaves. 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 were 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 (9–11 days gestation) exposed to microwaves at 10 mW/cm^2 incident power density at 2450 MHz for 90 min. 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- ones. 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. So, in summary, Nakamura et al. [82] showed that microwaves at the power of 10 mW/cm^2 produced activation of the hypothalamic–pituitary–adrenal axis and increased oestradiol in both virgin and pregnant rats, indicating that microwaves are a great stress in pregnancy.

In the following year, 1998, the same groups of scientists published a new study [83] in which they examined 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/cm^2 incident power density at 2450 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 °C for virgin and 0.9 °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, 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), Nakamura et al. published yet another study in 2000 [84]. In this article they measured these parameters and factors in rats exposed to continuous-wave (CW) microwave at 2 mW/cm^2 incident power density at 2450 MHz for 90 min. 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, 2450 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! [Could the above findings be part of the explanation behind the sensational findings of Magras and Xenos [85] from 1997?]

5.7.5. *Synchronization of cerebral rhythms. Important for the brain-immune system axis?*

Vecchio et al. [86] 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 deregulating the normal alpha wave 2 (about 8–10 Hz) and alpha 3 (10–12 Hz) bands. [Could such deregulation affect the brain-immune system axis? If so, what implications would it have in the short- as well as in the long-term?]

5.7.6. *Classical contact allergy reactions*

Finally, in addition, classical contact allergy reactions, such as chromate allergy, have been studied by Seishima et al. [87]. 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 eight patients with contact dermatitis possibly caused by handling a cellular phone. The eight patients were four males and four 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 seven had papules on the hemilateral auricle or in the preauricular region. Three of eight 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 eight 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.

6. Effects of electromagnetic fields on other biological systems

Some parallel investigations, pointing to severe biological effects that need to be mentioned are, for instance, the results of Roux et al. [88] in 2008. Using an especially designed facility, the Mode Stirred Reverberation Chamber, they exposed tomato plants (Lycopersicon esculentum Mill. VFN8) to low level (900 MHz, 5 V/m) EMF for a short period (10 min) and measured changes in abundance of three specific mRNA soon after exposure. Within minutes of stimulation, stress-related mRNA (calmodulin, calcium-dependent protein kinase and proteinase inhibitor) accumulated in a rapid, large and 3-phase manner typical of an environmental stress response. Accumulation of these transcripts into the polysomal RNA also took place (indicating that the encoded proteins were translated) but was delayed (indicating that newly-synthesized mRNA was not immediately recruited into polysomes). Transcript accumulation was maximal at normal Ca(2+) levels and was depressed at higher Ca(2+), especially for those encoding calcium-binding proteins. Removal of Ca(2+) (by addition of chelating agents or Ca(2+) channel blocker) led to total suppression of mRNA accumulation. Finally, 30 min after the electromagnetic treatment, ATP concentration and adenylate energy charge were transiently decreased, while transcript accumulation was totally prevented by application of the uncoupling reagent, CCCP. These responses occur very soon after exposure, strongly suggesting that they are the direct consequence of application of radiofrequency fields, and their similarities to wound responses strongly suggests that this radiation is perceived by plants as an injurious stimulus! [Furthermore, it is impossible to interpret these reactions as "psychological or psychiatric personality disturbances, cognitive malfunction, or likewise".]

Also, the data from Divan et al. [89] deserve to be mentioned. They examined the association between prenatal and postnatal exposure to cell phones and behavioral problems in young children. Mothers were recruited to the Danish National Birth Cohort early in pregnancy. When the children of those pregnancies reached 7 years of age in 2005 and 2006, mothers were asked to complete a questionnaire regarding the current health and behavioral status of children, as well as past exposure to cell phone use. Mothers evaluated the child's behavior problems using the Strength and Difficulties Questionnaire. Mothers of 13,159 children completed the follow-up questionnaire reporting their use of cell phones during pregnancy as well as current cell phone use by the child. Greater odds ratios for behavioral problems were observed for children who had possible prenatal or postnatal exposure to cell phone use. After adjustment for potential confounders, the odds ratio for a higher overall behavioral problems score was 1.80 (95% confidence interval = 1.45–2.23) in children with both prenatal and postnatal exposure to cell phones. Exposure to cell phones prenatally – and, to a lesser degree, postnatally – was associated with behavioral difficulties such as emotional and hyperactivity problems around the age of school entry. [An obvious follow-up question would be "What about immune function alterations?".] Naturally, and hopefully, these associations may be non-causal and may be due to unmeasured confounding. But if real, they would be of public health concern given the widespread use of this technology.

The exposure to non-thermal microwave EMF generated by mobile phones affects the expression of many proteins. This effect on transcription and protein stability can be mediated by the MAPK (mitogen-activated protein kinase) cascades, which serve as central signaling pathways and govern essentially all stimulated cellular processes. Indeed, long-term exposure of cells to mobile phone irradiation results in the activation of p38 as well as the ERK (extracellular signal-regulated kinase) MAPKs. Friedman et al. [90] recently have studied the immediate effect of irradiation on the MAPK cascades, and found that ERKs, but not stress-related MAPKs, are rapidly activated in response to various frequencies and intensities. Using signaling inhibitors, they delineated the mechanism that is involved in this activation. They found that the first step is mediated in the plasma membrane by NADH oxidase, which rapidly generates ROS (reactive oxygen species). These ROS then directly stimulate MMPs (matrix metalloproteinases) and allow them to cleave and release Hb-EGF (heparin-binding EGF (epidermal growth factor)). This secreted factor activates the EGF receptor, which in turn further activates the ERK cascade. Thus, their study demonstrates for the first time a detailed molecular mechanism by which electromagnetic irradiation from mobile phones induces the activation of the ERK cascade and thereby induces transcription and other cellular processes.

The terminal deoxynucleotide transferase dUTP nick end labeling (TUNEL) assay, a well known technique widely used for detecting fragmented DNA in various types of cells, was used by Panagopoulos et al. [91] to detect cell death (DNA fragmentation) in a biological model, the early and mid stages of oogenesis of the insect *Drosophila melanogaster*. The flies were exposed in vivo to either GSM 900 MHz or DCS 1800 MHz radiation from a common digital mobile phone, for few minutes per day during the first 6 days of their adult life. The exposure conditions were similar to those to which a mobile phone user is exposed. Previous results from the same group [92–94] had shown a large decrease in the oviposition of the same insect caused by GSM radiation. The recent results suggest that this decrease in oviposition, is due to degeneration of large numbers of egg chambers after DNA fragmentation of their constituent cells, induced by both types of mobile telephony radiation. Induced cell death is recorded for the first time, in all types of cells constituting an egg chamber (follicle cells, nurse cells and the oocyte) and in all stages of the early and mid-oogenesis, from germarium to stage 10, during which programmed cell death does not physiologically occur. Germarium and stages 7–8 were found to be the most sensitive developmental stages also in response to electromagnetic stress induced by the GSM and DCS fields and, moreover, germarium was found to be even more sensitive than stages 7–8.

7. Conclusions

- Both human and animal studies report large immunological changes upon exposure to environmental levels of modern, human-made EMFs. Some of these exposure levels are equivalent to those of wireless technologies in daily life, and often at low or very low (i.e., non-thermal) levels.
- 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. The data presented here, as well as the very rapid international increase in incidence of allergies, asthma and other oversensitivities, together form a clear warning signal.
- It is, thus, 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 area that should be investigated immediately.
- Specific findings from studies on exposures to various types of modern equipment and/or EMFs report overreaction 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 which 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 disfunction); suppressed or impaired immune function; and inflammatory responses that can ultimately result in cellular, tissue and organ damage.
- The functional impairment electrohypersensitivity is reported by individuals in the United States, Sweden, Switzerland, Germany, Belgium, Italy, The Netherlands, Norway, Denmark and many other countries of the world. Estimates range from 3% to perhaps 10% of populations, and appear 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.
- 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 literature. Also the accessability needs of persons with the functional impairment electrohypersensitivity must be fully addressed and resolved as dictated by the UN 22 "Standard rules on the equalization of opportunities for people with disabilities" (about the UN 22 Standard Rules, see website: http://www.un.org; since 2007 they have been upgraded into the UN "Convention on Human Rights for Persons with Functional Impairments").

The conclusion of the above must be that there are a number of very strong indications of EMFs being capable of disturbing the immune system and thus increasing disease, including cancer, risk. It is somewhat odd that professional epidemiologists for the last 50 years have not addressed the issue of reduced repair but only looked at increased cell damages from different agents and environments when trying to understand trend changes.

Based on this review as well as on the recent Bioinitiative Report [http://www.bioinitiative.org/] [1], it must be concluded that the existing public safety limits are inadequate to protect public health. From a public health policy standpoint, new public safety limits, and limits on further deployment of untested technologies, are warranted.

New biologically based public and occupational exposure are recommended to address bioeffects and potential adverse health effects of chronic exposure. These effects are now widely reported to occur at exposure levels significantly below most current national and international limits. Therefore, biologically based exposure standards are needed to prevent disruption of normal body processes. Effects are

reported for DNA damage (genotoxicity that is directly linked to integrity of the human genome), cellular communication, cellular metabolism and repair, cancer surveillance within the body; and for protection against cancer and neurological diseases. Also reported are neurological effects including changes in brainwave activity during cell phone calls, impairment of memory, attention and cognitive function; sleep disorders, cardiac effects; and – as reported here – serious impact on the immune function (allergic and inflammatory responses).

The current recommendation must be a biologically based exposure limit that is completely protective against e.g. extremely low frequency and radiofrequency fields which, with chronic exposure, can reasonably be presumed to result in no adverse impacts on health and well-being. Today, such a completely protective safety limit would, for many exposure situations, be zero.

Finally, attention to the above need would also mean a great gain in future public health costs for the entire electrified world. To do the opposite could turn out to be very expensive.

Acknowledgements

Supported by the Karolinska Institute, the Help Foundation (Hjälpfonden), Stiftelsen Tornspiran, and the Cancer and Allergy Foundation (Cancer- och Allergifonden). Ms Marianne Ekman is warmly acknowledged for her expert help with literature search engines, Mr. Philippe Hug for constructive criticism, and Mr. Jonas Aule for his superb technical support without which this paper would never have been completed.

References

[1] C.F. Blackman, M. Blank, M. Kundi, C. Sage, D.O. Carpenter, Z. Davanipour, D. Gee, L. Hardell, O. Johansson, H. Lai, K.H. Mild, A. Sage, E.L. Sobel, Z. Xu, G. Chen, The Bioinitiative Report—A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF), http://www.bioinitiative.org, 2007.

[2] B.R.R. Persson, L.G. Salford, A. Brun, Blood–brain barrier permeability in rats exposed to electromagnetic fields used in wireless communication, Wireless Networks 3 (1997) 455–461.

[3] L.G. Salford, A.E. Brun, J.L. Eberhardt, L. Malmgren, B.R. Persson, Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones, Environ. Health Perspect. 111 (2003) 881–883.

[4] O. Johansson, M. Hilliges, V. Björnhagen, K. Hall, Skin changes in patients claiming to suffer from "screen dermatitis": a two-case open-field provocation study, Exp. Dermatol. 3 (1994) 234–238.

[5] O. Johansson, S. Gangi, Y. Liang, K. Yoshimura, C. Jing, P.-Y. Liu, Cutaneous mast cells are altered in normal healthy volunteers sitting in front of ordinary TVs/PCs—results from open-field provocation experiments, J. Cutan. Pathol. 28 (2001) 513–519.

[6] V. Rajkovic, M. Matavulj, O. Johansson, Histological characteristics of cutaneous and thyroid mast cell populations in male rats exposed to power-frequency electromagnetic fields, Int. J. Radiat. Biol. 81 (2005) 491–499.

[7] V. Rajkovic, M. Matavulj, O. Johansson, The effect of extremely low-frequency electromagnetic fields on skin and thyroid amine- and peptide-containing cells in rats: an immunohistochemical and morphometrical study, Environ. Res. 99 (2005) 369–377.

[8] V. Rajkovic, M. Matavulj, O. Johansson, Light and electron microscopic study of the thyroid gland in rats exposed to power-frequency electromagnetic fields, J. Exp. Biol. 209 (2006) 3322–3328.

[9] M. Peakman, Basic and Clinical Immunology, Churchill Livingstone, New York, 2008.

[10] R.R.A. Coombs, P.G.H. Gell, P.J. Lachmann, Clinical Aspects of Immunology, Blackwell Scientific Publisher, Oxford, 1962.

[11] K. Jokela, L. Puranen, A.P. Sihvonen, Assessment of the magnetic field exposure due to the battery current of digital mobile phones, Health Phys. 86 (2004) 56–66.

[12] C. Sage, O. Johansson, S.A. Sage, Personal digital assistant (PDA) cell phone units produce elevated extremely-low frequency electromagnetic field emissions, Bioelectromagnetics 28 (2007) 386–392.

[13] O. Johansson, Electrohypersensitivity: state-of-the-art of a functional impairment, Electromagn. Biol. Med. 25 (2006) 245–258.

[14] R. Cox, Electrical hypersensitivity—human studies in the UK, in: Conference Presentation at the WHO International Workshop on EMF Hypersensitivity, Prague, Czech Republic, October 25–27, 2004.

[15] E. Fox, Electrosensitivity symptoms associated with electromagnetic field exposure, in: Conference Presentation at the WHO International Workshop on EMF Hypersensitivity, Prague, Czech Republic, October 25–27, 2004.

[16] P. Levallois, R. Neutra, G. Lee, L. Hristova, Study of self-reported hypersensitivity to electromagnetic fields in California, Environ. Health Perspect. 110 (4) (2002) 619–623.

[17] Institut für angewandte Sozialwissenschaft GmbH (infas)/Bundesamt für Strahlenschutz, Ermittlung der Befürchtungen und Ängste der breiten Öffentlichkeit hinsichtlich möglicher Gefahren der Hochfrequenten Elektromagnetischen Felder der Mobilfunks–Jährliche Umfrage, http://www.infas.de, 2004.

[18] J. Schüz, C. Petters, U.T. Egle, B. Jansen, R. Kimbel, S. Letzel, W. Nix, L.G. Schmidt, L. Vollrath, The "Mainzer EMF-Wachhund": results from a watchdog project on self-reported health complaints attributed to exposure to electromagnetic fields, Bioelectromagnetics 27 (2006) 280–287.

[19] M. Roosli, M. Moser, Y. Baldinini, M. Meier, C. Braun-Fahrlander, Symptoms of ill health ascribed to electromagnetic field exposure—a questionnaire survey, Int. J. Hyg. Environ. Health 207 (2004) 141–150.

[20] M. Roosli, Conference Poster at the WHO International Workshop on EMF Hypersensitivity, Prague, Czech Republic, October 25–27, 2004 [as reported in Rapporteur's Report by KH Mild], 2004.

[21] E. Lyskov, K.H. Mild, M. Sandstrom, Sensor Reactivity and Autonomous Regulation in Persons with Perceived Electrical Hypersensitivity. Conference Presentation at the WHO International Workshop on EMF Hypersensitivity, Prague, Czech Republic, October 25–27, 2004.

[22] C.H. Mueller, C. Schierz, Project NEMESIS: double blind study on effects of 50 Hz EMF on sleep quality, physiological parameters and field perception in people suffering from electrical hypersensitivity, in: K.H. Mild, M. Repacholi, E. van Deventer, P. Ravazzani (Eds.), Proceedings of the International Workshop on EMF Hypersensitivity, Prague, Czech Republic, 2004, pp. 107–121.

[23] E. Markovà, L. Hillert, L. Malmgren, B.R. Persson, I.Y. Belyaev, Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons, Environ. Health Perspect. 113 (2005) 1172–1177.

[24] I.Y. Belyaev, E. Markovà, L. Hillert, L.O. Malmgren, B.R. Persson, Microwaves from UMTS/GSM mobile phones induce long-lasting inhibition of 53BP1/gamma-H2AX DNA repair foci in human lymphocytes, Bioelectromagnetics 30 (2009) 129–141.

[25] A.P. Fews, D.L. Henshaw, P.A. Keitch, J.J. Close, R.J. Wilding, Increased exposure to pollutant aerosols under high voltage power lines, Int. J. Radiat. Biol. 75 (1999) 1505–1521.

[26] A.P. Fews, D.L. Henshaw, R.J. Wilding, P.A. Keitch, Corona ions from powerlines and increased exposure to pollutant aerosols, Int. J. Radiat. Biol. 75 (1999) 1523–1531.
[27] G. Nordström, The Invisible Disease—The Dangers of Environmental Illnesses caused by Electromagnetic Fields and Chemical Emissions, O Books, Hants and New York, 2004, ISBN 1-903816-71-8.
[28] O. Johansson, P.-Y. Liu, "Electrosensitivity", "electrosupersensitivity" and "screen dermatitis": preliminary observations from on-going studies in the human skin, in: D. Simunic (Ed.), Proceedings of the COST 244: Biomedical Effects of Electromagnetic Fields – Workshop on Electromagnetic Hypersensitivity. Brussels/Graz: EU/EC (DG XIII), 1995, pp. 52–57.
[29] X. Zhuang, A.J. Silverman, R. Silver, Distribution and local differentiation of mast cells in the parenchyma of the forebrain, J. Comp. Neurol. 408 (1999) 477–488.
[30] O. Johansson, M. Hilliges, S.W. Han, A screening of skin changes, with special emphasis on neurochemical marker antibody evaluation, in patients claiming to suffer from screen dermatitis as compared to normal healthy controls, Exp. Dermatol. 5 (1996) 279–285.
[31] S. Gangi, O. Johansson, Skin changes in "screen dermatitis" versus classical UV- and ionizing irradiation-related damage—similarities and differences. Two neuroscientists' speculative review, Exp. Dermatol. 6 (1997) 283–291.
[32] S. Gangi, O. Johansson, A theoretical model based upon mast cells and histamine to explain the recently proclaimed sensitivity to electric and/or magnetic fields in humans, Med. Hypotheses 54 (2000) 663–671.
[33] G. Holmboe, O. Johansson, Description of symptoms as well as occurrence of IgE and positive Phadiatop Combi in persons with the physical impairment electrohypersensitivity [Article in Swedish], Medicinsk Access 1 (2005) 58–63.
[34] D. Leszczynski, S. Joenväärä, J. Reivinen, R. Kuokka, Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: molecular mechanism for cancer- and blood–brain barrier-related effects, Differentiation 70 (2002) 120–129.
[35] R. Nylund, D. Leszczynski, Mobile phone radiation causes changes in gene and protein expression in human endothelial cell lines and the response seems to be genome- and proteome-dependent, Proteomics 6 (2006) 4769–4780.
[36] N. Wertheimer, E. Leeper, Electrical wiring configurations and childhood cancer, Am. J. Epidemiol. 109 (1979) 273–284.
[37] L. Hardell, Å. Näsman, A. Påhlson, A. Hallquist, K.H. Mild, Use of cellular telephones and the risk for brain tumours: a case–control study, Int. J. Oncol. 15 (1999) 113–116.
[38] L. Hardell, K.H. Mild, M. Carlberg, A. Hallquist, Cellular and cordless telephone use and the association with brain tumors in different age groups, Arch. Environ. Health 59 (2004) 132–137.
[39] L. Hardell, M. Carlberg, K.H. Mild, Case-control study on cellular and cordless telephones and the risk for acoustic neuroma or meningioma in patients diagnosed 2000–2003, Neuroepidemiology 25 (2005) 120–128.
[40] S. Lonn, A. Ahlbom, P. Hall, M. Feychting, Mobile phone use and the risk of acoustic neuroma, Epidemiology 15 (2004) 653–659.
[41] Ö. Hallberg, O. Johansson, Melanoma incidence and frequency modulation (FM) broadcasting, Arch. Environ. Health 57 (2002) 32–40.
[42] Ö. Hallberg, O. Johansson, Malignant melanoma of the skin—not a sunshine story!, Med. Sci. Monit. 10 (2004) CR336–CR340.
[43] Ö. Hallberg, O. Johansson, FM broadcasting exposure time and malignant melanoma incidence, Electromagn. Biol. Med. 24 (2005) 1–8.
[44] R. Anane, M. Geffard, M. Taxile, D. Bodet, B. Billaudel, P.E. Dulou, B. Veyret, Effects of GSM-900 microwaves on the experimental allergic encephalomyelitis (EAE) rat model of multiple sclerosis, Bioelectromagnetics 24 (2003) 211–213.
[45] P. Boscol, M.B. Di Sciascio, S. D'Ostilio, A. Del Signore, M. Reale, P. Conti, P. Bavazzano, R. Paganelli, M. Di Gioacchino, Effects of electromagnetic fields produced by radiotelevision broadcasting stations on the immune system of women, Sci. Total Environ. 273 (2001) 1–10.
[46] A. Dmoch, P. Moszczynski, Levels of immunoglobulin and subpopulations of T lymphocytes and NK cells in men occupationally exposed to microwave radiation in frequencies of 6–12 GHz [Article in Polish], Med. Pr. 49 (1998) 45–49.
[47] P. Moszczynski, J. Lisiewicz, A. Dmoch, Z. Zabinski, L. Bergier, M. Rucinska, U. Sasiadek, The effect of various occupational exposures to microwave radiation on the concentrations of immunoglobulins and T lymphocyte subsets [Article in Polish], Wiad. Lek. 52 (1999) 30–34.
[48] H. Tuschl, G. Neubauer, H. Garn, K. Duftschmid, N. Winker, H. Brusl, Occupational exposure to high frequency electromagnetic fields and its effect on human immune parameters, Int. J. Occup. Med. Environ. Health 12 (1999) 239–251.
[49] A. Del Signore, P. Boscolo, S. Kouri, G. Di Martino, G. Giuliano, Combined effects of traffic and electromagnetic fields on the immune system of fertile atopic women, Ind. Health 38 (2000) 294–300.
[50] S.F. Cleary, L.M. Liu, R.E. Merchant, In vitro lymphocyte proliferation induced by radio-frequency electromagnetic radiation under isothermal conditions, Bioelectromagnetics 11 (1990) 47–56.
[51] S.F. Cleary, Z. Du, G. Cao, L.M. Liu, C. McCrady, Effect of isothermal radiofrequency radiation on cytolytic T lymphocytes, FASEB J. 10 (1996) 913–919.
[52] E.M. Czerska, E.C. Elson, C.C. Davis, M.L. Swicord, P. Czerski, Effects of continuous and pulsed 2450-MHz radiation on spontaneous lymphoblastoid transformation of human lymphocytes in vitro, Bioelectromagnetics 13 (1992) 247–259.
[53] M.P. Dabrowski, W. Stankiewicz, R. Kubacki, E. Sobiczewska, S. Szmigielski, Immunotropic effects in cultured human blood mononuclear cells pre-exposed to low-level 1300 MHz pulse-modulated microwave field, Electromagn. Biol. Med. 22 (2003) 1–13.
[54] M.P. Dabrowski, W. Stankiewicz, E. Sobiczewska, S. Szmigielski, Immunotropic effects of electromagnetic fields in the range of radio- and microwave frequencies [Article in Polish], Pol. Merkur. Lekarski 11 (2001) 447–451.
[55] W. Stankiewicz, M.P. Dabrowski, R. Kubacki, E. Sobiczewska, S. Szmigielski, Immunotropic influence of 900 MHz microwave GSM signal on human blood immune cells activated in vitro, Electromagn. Biol. Med. 25 (2006) 45–51.
[56] M. Donnellan, D.R. McKenzie, P.W. French, Effects of exposure to electromagnetic radiation at 835 MHz on growth, morphology and secretory characteristics of a mast cell analogue, RBL-2H3, Cell. Biol. Int. 21 (1997) 427–439.
[57] C. Harvey, P.W. French, Effects on protein kinase C and gene expression in a human mast cell line, HMC-1, following microwave exposure, Cell. Biol. Int. 23 (2000) 739–748.
[58] E. Elekes, G. Thuroczy, L.D. Szabo, Effect on the immune system of mice exposed chronically to 50 Hz amplitude-modulated 2.45 GHz microwaves, Bioelectromagnetics 17 (1996) 246–248.
[59] E.E. Fesenko, E.G. Novoselova, N.V. Semiletova, T.A. Agafonova, V.B. Sadovnikov, Stimulation of murine natural killer cells by weak electromagnetic waves in the centimeter range [Article in Russian], Biofizika 44 (1999) 737–741.
[60] E.E. Fesenko, V.R. Makar, E.G. Novoselova, V.B. Sadovnikov, Microwaves and cellular immunity. I. Effect of whole body microwave irradiation on tumor necrosis factor production in mouse cells, Bioelectrochem. Bioenerg. 49 (1999) 29–35.
[61] A.B. Gapeev, V.G. Safronova, N.K. Chemeris, E.E. Fesenko, Modification of the activity of murine peritoneal neutrophils upon exposure to millimeter waves at close and far distances from the emitter [Article in Russian], Biofizika 41 (1996) 205–219.
[62] L. Gatta, R. Pinto, V. Ubaldi, L. Pace, P. Galloni, G.A. Lovisolo, C. Marino, C. Pioli, Effects of in vivo exposure to GSM-modulated 900 MHz radiation on mouse peripheral lymphocytes, Radiat. Res. 160 (2003) 600–605.
[63] M.P. Kolomytseva, A.B. Gapeev, V.B. Sadovnikov, N.K. Chemeris, Suppression of nonspecific resistance of the body under the effect of extremely high frequency electromagnetic radiation of low intensity [Article in Russian], Biofizika 47 (2002) 71–77.

[64] K.V. Lushnikov, A.B. Gapeev, V.B. Sadovnikov, N.K. Cheremis, Effect of extremely high frequency electromagnetic radiation of low intensity on parameters of humoral immunity in healthy mice [Article in Russian], Biofizika 46 (2001) 753–760.

[65] K.S. Nageswari, K.R. Sarma, V.S. Rajvanshi, R. Sharan, M. Sharma, V. Barathwal, V. Singh, Effect of chronic microwave radiation on T cell-mediated immunity in the rabbit, Int. J. Biometeorol. 35 (1991) 92–97.

[66] F. Nasta, M.G. Prisco, R. Pinto, G.A. Lovisolo, C. Marino, C. Pioli, Effects of GSM-modulated radiofrequency electromagnetic fields on B-cell peripheral differentiation and antibody production, Radiat. Res. 165 (2006) 664–670.

[67] E.T. Novoselova, E.E. Fesenko, Stimulation of production of tumor necrosis factor by murine macrophages when exposed in vio and in vitro to weak electromagnetic waves in the centimeter range [Article in Russian], Biofizika 43 (1998) 1132–1333.

[68] E.G. Novoselova, E.E. Fesenko, V.R. Makar, V.B. Sadovnikov, Microwaves and cellular immunity. II. Immunostimulating effects of microwaves and naturally occurring antioxidant nutrients, Bioelectrochem. Bioenerg. 49 (1999) 37–41.

[69] N. Çetin, A. Bilgili, G. Eraslan, Effects of pulsed magnetic field chronic exposure on some hematological parameters in mice, Revue Méd. Vét. 157 (2006) 68–71.

[70] K.I. Obukhan, The effect of ultrahigh-frequency radiation on adaptation thresholds and the damages to blood system cells [Article in Ukrainian], Lik. Sprava 7 (1998) 71–73.

[71] L. Stronati, A. Testa, J. Moquet, A. Edwards, E. Cordelli, P. Villani, C. Marino, A.M. Fresegna, M. Appolloni, D. Lloyd, 935 MHz cellular phone radiation. An in vitro study of genotoxicity in human lymphocytes, Int. J. Radiat. Biol. 82 (2006) 339–346.

[72] J.L. Phillips, O. Ivaschuk, T. Ishida-Jones, R.A. Jones, M. Campbell-Beachler, W. Haggren, DNA damage in Molt-4 T-lymphoblastoid cells exposed to cellular telephone radiofrequency fields in vitro, Bioelectrochem. Bioenerg. 45 (1998) 103–110.

[73] S. Ivancsits, E. Diem, A. Pilger, H.W. Rüdiger, O. Jahn, Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts, Mutat. Res. 519 (2002) 1–13.

[74] H. Lai, N.P. Singh, Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells, Bioelectromagnetics 16 (1995) 207–210.

[75] H. Tuschl, W. Novak, H. Molla-Djafari, In vitro effects of GSM modulated radiofrequency fields on human immune cells, Bioelectromagnetics 27 (2006) 188–196.

[76] J.L. Chagnaud, B. Veyret, In vivo exposure of rats to GSM-modulated microwaves: flow cytometry analysis of lymphocyte subpopulations and of mitogen stimulation, Int. J. Radiat. Biol. 75 (1999) 111–113.

[77] B. Veyret, C. Bouthet, P. Deschaux, R. de Seze, M. Geffard, J. Joussot-Dubien, M. le Diraison, J.M. Moreau, A. Caristan, Antibody responses of mice exposed to low-power microwaves under combined, pulse-and-amplitude modulation, Bioelectromagnetics 12 (1991) 47–56.

[78] M. Capri, S. Salviolo, S. Altilia, F. Sevini, D. Remondini, P. Mesirca, F. Bersani, D. Monti, C. Franceschi, Age-dependent effects of *in vitro* radiofrequency exposure (mobile phone) on CD95+ T Helper human lymphocytes, Ann. N. Y. Acad. Sci. 1067 (2006) 493–499.

[79] A.I. Yurekli, M. Ozkan, T. Kalkan, H. Saybasili, H. Tuncel, P. Atukeren, K. Gumustas, S. Seker, GSM base station electromagnetic radiation and oxidative stress in rats, Electromagn. Biol. Med. 25 (2006) 177–188.

[80] C. Schwarz, E. Kratochvil, A. Pilger, N. Kuster, F. Adlkofer, H.W. Rüdiger, Radiofrequency electromagnetic fields (UMTS 1 950 MHz) induce genotoxic effects in vitro in human fibroblasts but not in lymphocytes, Int. Arch. Occup. Environ. Health 81 (2008) 755–767.

[81] M. Simkó, M.O. Mattsson, Extremely low frequency electromagnetic fields as effectors of cellular responses in vitro: possible immune cell activation, J. Cell. Biochem. 93 (2004) 83–92.

[82] H. Nakamura, T. Seto, H. Nagase, M. Yoshida, S. Dan, K. Ogino, Effects of exposure to microwaves on cellular immunity and placental steroids in pregnant rats, Occup. Environ. Med. 54 (1997) 676–680.

[83] H. Nakamura, T. Seto, K. Hatta, I. Matsuzaki, H. Nagase, M. Yoshida, K. Ogino, Natural killer cell activity reduced by microwave exposure during pregnancy is mediated by opioid systems, Environ. Res. 79 (1998) 106–113.

[84] H. Nakamura, H. Nagase, K. Ogino, K. Hatta, I. Matsuzaki, Uteroplacental circulatory disturbance mediated by prostaglandin F(2alpha) in rats exposed to microwaves, Reprod. Toxicol. 14 (2000) 235–240.

[85] I.N. Magras, T.D. Xenos, RF radiation-induced changes in the prenatal development of mice, Bioelectromagnetics 18 (1997) 455–461.

[86] F. Vecchio, C. Babiloni, F. Ferreri, G. Curcio, R. Fini, C. Del Percio, P.M. Rossini, Mobile phone emission modulates interhemispheric functional coupling of EEG alpha rhythms, Eur. J. Neurosci. 25 (2007) 1908–1913.

[87] M. Seishima, Z. Oyama, M. Oda, Cellular phone dermatitis with chromate allergy, Dermatology 207 (2003) 48–50.

[88] D. Roux, A. Vian, S. Girard, P. Bonnet, F. Paladian, E. Davies, G. Ledoigt, High frequency (900 MHz) low amplitude (5 V/m) electromagnetic field: a genuine environmental stimulus that affects transcription, translation, calcium and energy charge in tomato, Planta 227 (2008) 883–891.

[89] H.A. Divan, L. Kheifets, C. Obel, J. Olsen, Prenatal and postnatal exposure to cell phone use and behavioral problems in children, Epidemiology 19 (2008) 523–529.

[90] J. Friedman, S. Kraus, Y. Hauptman, Y. Schiff, R. Seger, Mechanism of short-term ERK activation by electromagnetic fields at mobile phone frequencies, Biochem. J. 405 (2007) 559–568.

[91] D.J. Panagopoulos, E.D. Chavdoula, I.P. Nezis, L.H. Margaritis, Cell death induced by GSM 900-MHz and DCS 1800-MHz mobile telephony radiation, Mutat. Res. 626 (2007) 69–78.

[92] D.J. Panagopoulos, L.H. Margaritis, Effects of electromagnetic fields on the reproductive capacity of *D. melanogaster*, in: P. Stavroulakis (Ed.), Biological Effects of Electromagnetic Fields, Springer, Berlin/New York, 2003, pp. 545–578.

[93] D.J. Panagopoulos, N. Messini, A. Karabarbounis, A.L. Philippetis, L.H. Margaritis, Radio frequency electromagnetic radiation within "safety levels" alters the physiological function of insects, in: P. Kostarakis, P. Stavroulakis (Eds.), Proceedings of the Millennium International Workshop on Biological Effects of Electromagnetic Fields, Heraklion, Crete, Greece, 2000, pp. 169–175.

[94] D.J. Panagopoulos, A. Karabarbounis, L.H. Margaritis, Effect of GSM 900-MHz mobile phone radiation on the reproductive capacity of *D. melanogaster*, Electromagn. Biol. Med. 23 (2004) 29–43.

ELSEVIER

Pathophysiology 16 (2009) 179–189

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Reproductive and developmental effects of EMF in vertebrate animal models

Aris F. Pourlis *

Laboratory of Anatomy Histology & Embryology, Veterinary School, University of Thessaly Karditsa, Greece

Received 10 August 2008; received in revised form 28 August 2008; accepted 30 January 2009

Abstract

This paper reviews the literature data on the effects of electromagnetic fields (EMF), in the reproductive organs as well as in prenatal and postnatal development of vertebrate animals. Review articles which have been published till 2001, regarding the reproductive and developmental effects of the entire range of frequency of electromagnetic fields, were surveyed. Experimental studies which were published from 2001 onwards were summarized. Special focus on the effects of radiofrequencies related to mobile communication in the above mentioned topics has been made. According to the majority of the investigations, no strong effects resulted regarding the exposure to EMF of mobile telephony in the animal reproduction and development. However further research should be done in order to clarify many unknown aspects of the impact of EMF in the living organisms.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Electromagnetic fields (EMF); Mobile phones; Teratology; Endometrium; Testis

1. Introduction

During the 20th century, the exposure to electromagnetic fields (EMF) became an important source of concern about the possible effects in the living organisms. The artificial sources of electromagnetic radiation have risen tremendously because of the ongoing needs on electricity, telecommunications, and electronic devices. In this context, World Health Organisation (WHO) established in 1996 the International EMF project in order to assess health and environmental effects of exposure to EMF in the frequency range from 0 to 300 GHz. For the purpose of this paper this range will be divided into static (0 Hz), extremely low frequency (ELF > 0–300 kHz), intermediate frequencies (IF > 300–10 MHz) and radiofrequency (RF 10 MHz–300 GHz) fields [J. Juutilainen, Developmental effects of electromagnetic fields, Bioelectromagnetics 7 (2005) S107–S115]. The mobile phone technology is based on radiofrequency radiation with transmission of microwaves carrying frequencies between 880 and 1800 MHz [P.A. Valberg, T.E. van Deventer, M.H. Repacholi, Workgroup report: base stations and wireless networks-radiofrequency (RF) exposures and health consequences, Environ. Health Perspect. 115 (2007) 416–424].

The mobile telephony revolution took place in the last decade. There is an increasing number of cell phone users all over the world. Also, new technologies which use the spectrum of high frequency emissions are incorporated in many aspects of telecommunications. As a consequence, there is a lot of interest about the possible effects of the radiation emitted from the machines which are engaged in the telephony such as hand phones, base stations and transmitters.

The biological effects of EMF have been and are being investigated on different levels of organization. On the level of human populations, epidemiological studies are used whereas, on the level of individuals human, animal and plant *in vivo* experiments are carried out. Furthermore, on the level of organs, tissues and cells *in vitro* investigations are employed. Finally, on the sub-cellular level, biochemical and molecular techniques are utilized.

From another point of view, many studies have been carried out or are in progress about the various effects of radiation emissions regarding the behaviour, cancer, central nervous system, sleep, children, cardiovascular system, immune function, reproduction and development [3].

* Tel.: +30 24410 66013.
E-mail address: apourlis@vet.uth.gr.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.010

The present paper will focus on the existing data about the reproductive and developmental effects of EMF in vertebrates. Reproduction is a critical function of the organisms and involves two body systems the male and female genital system. The development comprises a series of events which begins with fertilization, continues with implantation, embryonic growth and terms with sexual maturity. In the context of systematic zoology, the vertebrates are close to the humans. Therefore, the animal studies could provide useful information on the comprehension of interaction of EMF with the living organism and on the possible commonality with the humans.

The biological effects of EMF of interest can be broadly grouped into thermal and non-thermal [4]. The thermal effects are associated with local heat production just like the mechanism of a microwave oven. The non-thermal mechanism is triggered by an amount of energy absorption, which is not directly associated with temperature change but rather to some other changes produced in the tissues.

The goal of this paper is to present the up to date available data about the EMF and their potential effects on reproduction and development, filling the gap of information from the most recent published reviews. All the bibliographic data which will be presented were collected exclusively from scientific journals published in English and partially in other languages. The survey includes studies which were published from 2001 onward. The studies which relate to the impact of mobile phone electromagnetic fields will be presented thoroughly and independently from the date of their publication.

2. Historical background

The first paper which I found in the medical literature, regarding the effects of EMF on the development of vertebrates, was published in 1893 in an anatomical journal from Windle [5]. The author summarized the observations of three scientists and added his own about the effects of electricity on the chicken embryos. Two years later the same author [6], published an account on the effects of electricity and magnetism on development.

In 1980 two papers were published about the biological effects of microwave radiation. Cook et al. [7] published a comprehensive survey regarding the very early research on the biological effects of electromagnetic fields. The early work on short waves from 1885 to 1940 was presented. Following, the authors summarized the available data from 1940 to 1960. Leach [8] provided an account on the genetic, growth and reproductive effects of microwave radiation including early studies in this field that were published from 1959 to 1979. The majority of revised papers dealt with animals. Later, Algers and Hennichs [9] summarized the biological effects on vertebrates, of electromagnetic fields where the frequency did not exceed 100 Hz. The authors included many studies about the impact of EMF on farm animals. The same year, a specialized review was published on the effects of non-ionizing radiation on birds [10].

Berman et al. [11], presented the results of a large multinational experimental effort (Henhouse project) regarding the low frequency EMF effects on chick embryos. Juutilainen [12], Chernoff et al. [13], Brent et al. [14] presented detailed reviews of the literature about the effects on reproduction related to low frequency EMF.

Jensh [15] reviewed behavioral teratologic studies using microwave radiation with special interest to continuous wave (CW) 915, 2450, or 6000 MHz radiation.

Verschaeve and Maes [16] reviewed the genetic, carcinogenic and teratogenic effects of RF (300 MHz–300 GHz). Regarding the effects on reproduction and teratogenesis, studies from 1961 to 1991 were surveyed. The majority of these experimental studies dealt with the exposure of animals at 2.45 GHz. The same year, Huuskonen et al. [17] reported on the teratogenic and reproductive effects of low frequency (0–100 kHz) magnetic fields associated with the use or transmission of electric power or emitted from video display terminals. The animal studies that were surveyed, have been published from 1987 to 1997 regarding the effects of alternating magnetic fields on prenatal development of rats and mice. In the same paper, studies on the effects of prenatal exposure of alternating magnetic fields on postnatal development were included. Brent [18] provided a thorough review of *in vivo* and *in vitro* studies on the reproductive and teratologic effects of low frequency EMF. The survey of reproductive effects has involved studies with chick embryos, chickens, cows, mice, and rats from 1969 to 1996. O'Connor [19] recorded the intrauterine effects in animals exposed to radiofrequency and microwave fields with a special feature. The SAR of the surveyed studies was above the limit of 0.4 W/kg.

Experimental studies on the teratologic effects or developmental abnormalities from exposure to RF electromagnetic fields in the range 3 kHz–300 GHz were reviewed from Heynick and Merritt [20]. The review included investigations with insects, birds (chicken, quails, turkeys) and mammalian species (mice, rats) as well as non-human primates which appeared from 1974 to 2000. A brief critical review on the developmental effects of extremely low frequency (ELF) electric and magnetic fields provided by Juutilainen [21]. Löscher [22] published a survey of the effects of radiofrequency electromagnetic fields on production, health and behaviour of farm animals.

Juutilainen [1] reported on the effects of EMF on animal development. In his review, he surveyed specific topics such as the Henhouse project, the interaction of LF-IMF EMF with known teratogens, and the behavioral teratology of RF. Saunders and McCaig [23] summarized the possible effects on prenatal development of physiologically weak electric fields induced in the body by exposure to extremely low frequency electromagnetic fields and of elevated temperature levels that might result from exposure to radiofrequency (RF) radiation.

Table 1
Overview of investigations on EMF effects on animal genital system.

Animal species	Exposure frequency	Exposure parameters	Exposure duration	Endpoint	Results	Comments	Reference
Mouse Swiss	50 Hz	25 mT	Continuous 90 days	Effects on reproductive ability	No effect on the fertility of male and female mice. The ovarian weight was significantly increased		[27]
Mouse CD1 (BALB/c X DBA/2)	60 Hz	2 mT	Continuous for 72 h or 8 h/day for 10 days	Sperm morphology	No statistically differences were observed	Two groups were treated with mitomycin C. Sperm abnormalities were found in the group exposed versus the group treated with mitomycin C alone	[28]
Mouse BALB/c	60 Hz	0.1 or 0.5 mT	24 h/day for 8 weeks	Germ cell apoptosis in the testes	No significant changes in testicular weights. Decrease of normal seminiferous tubules. Increase of the germ cell death		[29]
Rat Sprague–Dawley	60 Hz	5, 83.3, 500 mT	Continuous 21 h/day from day 6 of gestation to day 21 of lactation	Spermatotoxicity and reproductive dysfunction inthe F1 offspring	No detectable alterations in offspring spermatogenesis and fertility		[30]
Rat Sprague–Dawley	50 Hz	$25 \pm 1\ \mu T$	Continuous for 18 weeks	Effects on sperm count, weights of testes, seminal vesicles, preputial glands	No effect on the weight of testes. Significant reduction of the weight of seminal vesicles and preputial glands. Significant reduction in sperm count		[31]
Rat Sprague–Dawley	50 Hz	1.35 ± 0.018 mT	2 h/day, 7days/week for 2 months	Sperm count, morphological changes of testes	No significant alterations were observed	Funding not mentioned	[32]
Rat Wistar albino♀♂	50 Hz	1 mT (mean value)	3 h/day for 50 or 100 days	Morphological evaluation of uterus and ovaries	Ultrastructural alterations in germinal epithelium of ovaries in the experimental group (50 days) as well as in tunica albuginea (100 days)	Ambiguous observations in the uterus	[33]
Rat Sprague–Dawley♂♀	20 kHz	6.25 mT	8 h/day, 5 days/week for 90 days	Histopathological examination of various organs	No differences were seen in testis and ovary		[34]

Table 1 (*Continued*)

Animal species	Exposure frequency	Exposure parameters	Exposure duration	Endpoint	Results	Comments	Reference
Rat Wistar ♂♀	50 Hz		3 weeks *in utero* and 5 weeks postnatal	Testes	Morphological changes in the boundary tissue of the seminiferous tubules		[35]
Rat Sprague–Dawley♀♂	20 kHz sine waves	6.25 mT	8 h/day for 12 or 18 months	Histopathological examination of various organs	No differences were seen in testis and ovary		[36]
Rat Wistar	30–300 GHz	>0.3 mW/cm^2	30 min for 63 days	Spermatogenesis	Morphological changes in spermatozoa	Scanty data presentation	[37]
Rat Wistar	50 Hz		8 h/day for 8 months	Histological evaluation of testes	Mean seminiferous tubule diameter and testicular weight were significantly lower in exposed group. Histologic damage score was threefold in experimental group versus control		[38]

A special topic, the effects of EMF from power lines on avian reproductive biology, was reviewed by Fernie and Reynolds [24]. Krewski et al. [25], reviewed studies referring to various disciplines regarding the effects of RF. The included literature was published between 2001 and 2003. A novelty of this paper, was a discussion of the reports of various authorities and committees about the potential health risks associated with exposure to RF fields. A gap in the literature regarding the biological effects of EMF in the intermediate frequency range was covered by the review of Shigemitsu et al. [26].

During the last decade, many reports from authorities (local, national and international) and expert panels have been uploaded on the web [2].

It is suggested that the reader refer to the above-mentioned review articles and electronic addresses, in order to assemble a more complete and detailed view of the biological effects of EMF.

3. Male genital system

The testes are very important organs situated externally to the body and enclosed by the scrotum. The testicular parenchyma is the site of an intense proliferation and differentiation of the germinal cells that will become the sperm cells. The testes are very sensitive to temperature variations and for this reason the scrotum, which contains the testicular parenchyma, has a specialized contractile structure.

Studies that have evaluated EMF effects (mainly LF) on the genital systems of the vertebrates are summarized in Table 1.

Regarding mobile telephony, the first study conducted by Dasdag et al. [39] investigated whether there are adverse effects due to microwave exposure emitted by cellular phones in male Wistar albino rats. The animals ($n = 18$) were divided in three groups (control, standby exposed group, speech exposed group). Specific energy absorption rate (SAR) was 0.141 W/kg. Rats in the experimental groups were exposed for 2 h/day for 1 month in standby position, whereas phones were turned to the speech position three times for 1 min. The decrease of epididymal sperm counts in the speech groups was not found to be significant. Differences in terms of normal and abnormal sperm forms were not observed. Histological changes were especially observed in the testes of rats in the speech group. Seminiferous tubular diameter of rat testes in the standby and speech groups was found to be lower than the sham group. Rectal temperatures of rats in the speech group were found to be higher than the sham and standby groups. The rectal temperatures of rats before and after exposure were also found to be significantly higher in the speech group.

The same group of authors [40], failed to reproduce the results of their previous work. Sixteen Sprague–Dawley rats were separated into two groups (control, experimental). They were exposed to 890–915 MHz pulsed wave (PW) daily for

20 min/day for 1 month. For 250 mW average radiated power, SAR was 0.52 W/kg. No differences were observed in the percentages of epididymal normal and abnormal sperms, the epididymal sperm count, as well as in the seminiferous tubule diameter between control and experimental groups. Also, the testicular biopsy score as evaluated by Johnson's scale did not differ significantly.

Aitken et al. [41] assessed the testis of mice irradiated with 900 MHz in a waveguide, with an exposure condition SAR 90 mW/kg for 7 days at 12 h/day. The authors did not observe abnormalities regarding the sperm number, morphology and vitality. However, they reported significant damage to the mitochondrial genome as well as to the nuclear-globin locus.

Results similar to a previous study [39] regarding the diameter of the seminiferous tubules of rat testes were obtained by Ozguner et al. [42]. During the experiment, 20 male Sprague–Dawley rats (5 months of age) were either exposed to 900 MHz CW (average power density $1 \pm 0.4\,\mathrm{mW/cm^2}$) or not (control group). Rats exposed 30 min/day, for 5 days/week for 4 weeks. The authors also did not observe significantly different values of weight of testes, testicular biopsy score count and the percentage of interstitial tissue. However, the mean height of the germinal epithelium was found decreased in the group of rats that had been irradiated.

Forgács et al. [43] repeatedly exposed male NMRI mice to 1800 MHz GSM like microwave radiation at 0.018–0.023 W/kg whole body SAR. 11–12 sham exposed and 11–12 exposed mice were used. The animals were exposed ten times (over 2 weeks) and the duration of exposure was 2 h/day. No microwave exposure-related morphological alterations were found in testis, epididymis and prostate.

Adult male rats were examined after exposure at subcrhronic exposure to RF emitted from a conventional cell phone on their testicular function. Sixteen Wistar rats were used at age 30 days. The animals were exposed for 1 h daily during 11 weeks. The experimental group ($n = 8$) was exposed to 1835–1850 MHz at $0.04–1.4\,\mathrm{mW/cm^2}$. Total body weight and absolute and relative testicular and epididymal weights did not change significantly. Epididymal sperm count was not significantly different between the groups. Regarding the histomorphological endpoints of the study, no difference was found between the experimental and control arm [44].

The effect of cellular phone emissions on sperm characteristics in 16 Sprague–Dawley rats were studied [45]. The laboratory animals were divided in two groups (experimental, control) and exposed to four cell phones which had a personal communications service code division multiple access frequency band of 1.9 GHz (800 MHz digital and 800 MHz analog). The rats received daily (3 h–30 min rest–3 h) cell phone exposure for 18 weeks. The SAR ranged from 0.9 to 1.80 W/kg whereas the power from 0.00001 to 0.607 W, according to the specific mode of function. The authors analyzed the morphology of the sperm cells from epididymis of rats. The percentage of deformities for the experimental group was 34.3% and the percentage of deformities for the control group was 32.1%. This difference in the occurrence of deformities between the two groups was not statistically significant ($p > .05$) through a paired t test. The total sperm counts from the testes were not significantly different between the two groups. None of the temperature differences between the two groups were statistically significant.

Sixteen Sprague–Dawley rats were used to evaluate the bcl-2 protein (an anti-apoptotic protein) in rat testes. The experimental group ($n = 8$) was exposed to commercial (GSM) cellular phones irradiation for 20 min/day for 1 month. Average power density was measured at $0.047\,\mathrm{mW/cm^2}$ and SAR levels changed between 0.29 and 0.87 W/kg. The testes were investigated by means of immunohistochemistry. No difference was observed between testes sections of the sham and experimental groups in terms of bcl-2 staining. These results indicate that the radiation emitted from 900 MHz cellular phones did not alter the anti-apoptotic protein in the testes of rats [46].

In order to investigate the apoptosis-inducing effect of mobile phone exposure on spermatogonia in seminiferous tubules, 31 Wistar albino male rats were divided in three groups such as cage control ($n = 10$), sham exposed ($n = 7$), and experimental ($n = 14$). The 2 h/day (7 days/week) exposure of 900 MHz radiation (power density $0.012–0.149\,\mathrm{mW/cm^2}$ and SAR 0.07–0.57 W/kg) over a period of 10 months was evaluated by means of immunohistochemistry. The long-term radiation did not affect the active caspace-3 levels in testes of rats. Caspace-3 is a typical feature of apoptosis [47].

4. Female genital system

Studies on the impact of RF in the female genital system are scarce. Two studies were conducted in order to evaluate the effects on endometrial apoptosis and the ameliorating effects of a combination of vitamin E and C against EMF damage.

Oral et al. [48], exposed sexually mature female rats (16 weeks old) to 900 MHz radiation, 30 min/day for 30 days. Twenty-four Wistar albino rats were divided in three groups (sham exposed, EMF exposed, EMF exposed treated with vitamin C and E). The animals were exposed at $1.04\,\mathrm{mW/cm^2}$ (SAR 0.016–4 W/kg). The effect of microwaves was examined in rat endometrium by means of immunohistochemistry. Endometrial apoptosis was observed. Guney et al. [49], repeated the experiment with the addition of another group (control). Histological changes in endometrium, diffuse and severe apoptosis in the endometrial surface, epithelial and glandular cells were reported regarding the group exposed to EMF. Also, eosinophilic leucocyte and lymphocyte infiltration were seen in the endometrial stroma.

Table 2
Overview of investigations on EMF effects on animal development.

Animal species	Exposure frequency	Exposure parameters	Exposure duration	Endpoint	Results	Comments	Reference
Rat Sprague–Dawley	50 Hz	7, 70, 350 mT	22 h/day during 0–7 or 8–15 day of gestation	Effects on teratogenicity and embryonic development	No differences regarding embryonic deaths, fetal weight and teratogenicity		[50]
Mouse ICR	50 Hz	Sham (0.1–1 μT), 0.5, 5 mT	9 weeks♂ 2 weeks♀ prior to mating	Effects on teratogenicity and embryonic development	No differences regarding embryonic deaths, fetal weight and teratogenicity		[51]
Mouse Swiss Webster	0 Hz–25 MHz		1 week beginning from the 18th day of pregnancy	Morphological changes in brain, thymus, adrenal gland during embryonic development	Pathological changes were observed in the neonates		[52]
Rat Sprague–Dawley	60 Hz	0 (sham group), 5, 83.3, 500 mT.	22 h/day during 6–20 day of gestation	Developmental toxicity	No differences regarding embryonic deaths, fetal weight and teratogenicity		[53]
Chicken	50 Hz	1.33–7.32 mT	24 h	Effects on teratogenicity and embryonic development	Significant difference in the percentage of abnormal embryos versus control was found in 4.19, 5.32, 5.86, and 6.65 densities. Some embryos with extra ribs, defects in ribs and vertebrae, anuria and abnormal beaks were observed	Funding not mentioned	[54]
Mouse ICR	20 kHz	6.5 mT	8 h/day from 2.5 to 15.5 days post-coitum	Effects on teratogenicity and embryonic development	No statistically significant differences in the number of implantation, embryonic death, resorption, growth retarded fetuses, external and skeletal abnormalities		[55]
Chicken Leghorn HR7	50 Hz	1 μT, 500 μT, 1 mT	Continuous for 15 or 21 days	Effects on embryo/fetus	At 15 days of incubation body weight was significantly lower versus controls. At 21 days of incubation the body weight and cranial diameters were smaller versus control. No differences in brain weight were observed in all groups	Funding not mentioned	[56]
Mouse ♀	Static magnetic field	400 mT	6 min/day from 7.5 to 14.5 day of pregnancy	Teratogenic effects	Polydactylism, abdominal fissure, fused ribs, vestigial 13th rib, brain hernia, curled tail		[57]
Mouse ♀	50 Hz	1.2 mT	8 h/day during pregnancy	Body weight of dams, development of offspring	Fetal loss, malformed fetuses, retardation of growth of the offspring in the first 2 weeks after birth	Article in chinese	[58]
Chicken White Leghorn eggs	50 Hz	1.33–7.32 mT	4 days	Morphological evaluation of embryos/fetuses	Abnormal brain cavities, spina bifida, monophthalmia, ocular defects and growth retardation		[59]

5. Developmental effects

The critical phases in the dynamic process of development take place mainly *in utero* (mammals) or *in ovo* (birds) i.e. during the embryonic period. The main bulk of investigations were performed regarding the possible effects on animals after irradiation, during *in utero* or *in ovo* development. The effects on development are determined by endpoints such as weight gain, congenital malformations, resorptions, and number of litters. These endpoints will be considered for various exposure conditions.The effects of EMF (mainly LF) on animal development are summarized in Table 2. Egg production was reduced (8%) when young laying hens have been continuously exposed to CW 915 MHz with an incident power of 800 mW during the first 2.5 weeks, 0 mW during the following week and 200 mW for the rest of experiment. Hatching of fertile and total eggs was not significantly influenced. No macroscopic malformations were observed in the chicks or dead embryos [60].

Jensh et al. [61] irradiated pregnant Wistar albino rats at a power density level of 10 mW/cm^2, at a frequency of 915 MHz and average SAR 3.57 W/kg. The animals were exposed for 6 h/day from day 1 to day 21 of gestation. No significant teratogenic signs were observed regarding the resorption rate, malformation rate, mean litter size, fetal weight and number of live and dead fetuses. The experiment was repeated and extended in order to analyze the embryonic and postnatal development of offspring [62]. Eleven pregnant rats were irradiated and 19 rats were used as control animals. All animals delivered and raised their offspring (F_{1a}) until weaning at 30 days of age. Ten days later females were rebred and teratologic evaluation was conducted on the resultant F_{1b} fetuses. At 90 days of age, reproductive capability was evaluated and a standard teratologic analysis performed on the resultant F_2 offspring. No significant morphologic changes were revealed.

Pregnant rats were exposed at 970 MHz for 22 h/day from the 1st to 19th day of pregnancy [63]. The SAR values varied from 0.07, 2.4 and 4.8 W/kg. The embryo mortality, fetal weight, skeletal ossification, as well as maternal fertility were evaluated. The exposure with SAR 4.8 W/kg caused reduced (−12%) fetal body weight versus the control. All the other examined parameters were not significantly different.

Klug et al. [64] exposed rat embryos (9.5 days old) for up to 36 h to 900 MHz. The modulation frequency was fixed at 215 Hz and the SAR values were calculated at 0.2, 1 and 5 W/kg. The endpoints of the experiment were crown-rump length, number of somites as well as embryonic malformations. No significant changes were observed on the growth and differentiation parameters of the embryos. Magras and Xenos [65] investigated the possible effects of radiofrequency radiation on prenatal development in mice. The study consisted of *in vivo* experiments at several places around an "antenna park" where the frequency emissions ranged from 88.5 to 950 MHz. At these locations RF power densities between 168 and 1053 nW/cm^2 were measured. Twelve pairs of mice, divided in two groups, were placed in locations of different power densities and were repeatedly mated five times. One hundred eighteen newborns were collected. They were measured, weighed, and examined macro- and microscopically. A progressive decrease in the number of newborns per dam was observed, which ended in irreversible infertility. The prenatal development of the newborns, however, evaluated by the crown-rump length, the body weight, and the number of the lumbar, sacral, and coccygeal vertebrae, was improved. Wistar albino rats [15] were exposed through pregnancy for 6 h each day to CW 915 MHz radiation at a power density level of 10 mW/cm^2. Teratologic evaluation included the following parameters: mean litter size, maternal organ weight and organ weight/body weight ratios, body weight ratios of various organs (brain, liver, kidneys, and ovaries), number of resorptions and resorption rate, number of abnormalities and abnormality rate, mean term fetal weight. Mothers were rebred, and the second, unexposed litters were evaluated for teratogenic effects. Animals exposed to 915 MHz did not exhibit any consistent significant alterations in any of the above parameters.

Wistar rats were continuously exposed [66] during pregnancy to a low-level (0.1 mW/cm^2) 900 MHz, 217 Hz pulse modulated EMF. Whole body average SAR values for the freely roaming, pregnant animals were measured in models; they ranged between 17.5 and 75 mW/kg. No differences between exposed and sham exposed dams or offspring were recorded in terms of litter size, evolution of body mass and developmental landmarks of litter mates. The effects of microwaves emitted by cellular phones on birth weights of rats were investigated by Dasdag et al. [67]. Thirty-six Wistar albino rats were divided into four groups. Each experimental or sham exposed group comprised six males or 12 females. The rats were exposed at 890–915 MHz (SAR 0.155 W/kg). Males were exposed daily for 3 × 1 min during 2 h/day for 1 month. Females were exposed in the same way until they gave birth. When the offspring became adult the experiment was repeated on them. No significant differences were observed between rectal temperatures in the sham and experimental groups. The birth weight of offspring in the experimental group was significantly lower than in the sham exposed group. However in the next generation of rats all parameters investigated were normal. Pregnant Sprague–Dawley rats were exposed [68] to ultra wide band (UWB) 0.1–1 GHz radiation in order to determine if teratological changes occur in rat pups as a result of (1) daily UWB exposures during gestation days 3 ± 18, or (2) as a result of both prenatal and postnatal (10 days) exposures. Dams were exposed either to (I) UWB irradiation with average whole body specific absorption rate 45 mW/kg (II) sham irradiation or (III) a positive control. Offspring were examined regarding litter size, sex-ratios, weights, coat appearance, and tooth eruption. The pups postnatally exposed were examined for hippocampal morphology. Generally, no significant differences were found between the exposed and sham group. The medial-to-lateral length of the hippocampus was significantly longer in the

Table 3
Summary of animal studies on effects of EMF (related to mobile telephony), on reproduction and development.

Animal species	Exposure frequency	Endpoint	Effect	Reference
Chicken	915 MHz	Development	No	[60]
Rat	915 MHz	Development	No	[61]
Rat	915 MHz	Development	No	[62]
Rat	970 MHz	Development	No	[63]
Rat	915 MHz	Development	No	[15]
Rat	900 MHz	Development	No	[64]
Mouse	88.5–950 MHz	Fertility/development	Yes/no	[65]
Rat	890–915 MHz	Testes	Yes	[39]
Rat	900 MHz	Development	No	[66]
Rat	0.1–1 GHz	Development	No	[68]
Rat	890–915 MHz	Development	Yes	[67]
Chicken	900 MHz	Development	Yes	[69]
Rat	890–915 MHz	Testes	No	[40]
Chicken		Development	Yes	[70]
Rat	900 MHz	Testes	No	[42]
Mouse	900 MHz	Testes	No	[41]
White stork	900–1800 MHz phone mast	Reproduction	Yes	[74]
Chicken	900 MHz	Kidney development	Yes	[71]
Mouse	1800 MHz	Testes	No	[43]
Rat	900 MHz	Endometrium	Yes	[48]
Rat	900 MHz	Brain development	No	[72]
Rat	1835–1850 MHz	Testes	No	[44]
Rat	1.9 GHz	Sperm	No	[45]
Tit	1200–3000 MHz	Reproduction	No	[75]
Rat	900 MHz	Endometrium	Yes	[49]
Chicken	900 MHz	Development	Yes	[73]
Rat	900 MHz	Testes	No	[46]
Rat	900 MHz	Testes	No	[47]

UWB-exposed pups than in the sham exposed animals but could not correlated with neurological dysfunction. The male offspring exposed *in utero* to UWB mated significantly less frequently than sham exposed males, but when they did mate there was no difference in fertilization and offspring numbers from the sham group.

Bastide et al. [69] reported chicken embryo mortality from day 7 to day 11 of incubation. This mortality reached 64% compared to 11% in controls. The maximum level of embryonic mortality was observed in the eggs placed near the telephone.

Chicken embryos were exposed to EMF from GSM mobile phone during the embryonic development [70]. The embryo mortality rate in the incubation period increased to 75% versus 16% in control group.

Ingole and Ghosh [71] studied by means of light microscopy the developmental effects on the avian kidney of radiation, from a cell phone handset (900 MHz frequency, power of 2 W and SAR of 0.37 W/kg). The authors reported morphological alterations on the epithelium of the renal tubules as well as of the renal corpuscles in E6, E8 and E10 chicken embryos.

The possible impact of cell phone radiation in the developing central nervous system of male Wistar rats was examined [72]. The animals were exposed to 900 MHz signal for 2 h/day on 5 days/week. After 5 weeks of exposure at whole body average SAR of 0.3 or 3 W/kg or sham exposure no degenerative morphological changes were found.

The results about the effects of exposing fertilized chicken eggs to a mobile phone over the entire period of incubation were published recently [73]. In this study, a series of 4 incubations were employed. During each incubation, 4 groups were used (control I, control II, experimental, sham). In the experimental group, the cell phone in call position was placed near ($\leq$25 cm) the eggs, whereas in the sham group the cell phone in off position was placed 1.5 m away from the exposed group. A significantly higher percentage of embryo mortality was observed in the experimental compared to the sham group in 2 of the 4 incubations. The lethal effects of embryo development in the experimental group were mainly observed between the 9th and 12th day of incubation.

Another issue that in recent years has attracted the attention of scientists is the effects of radiation from RF antennas on the biology of wild birds.

Balmori [74] investigated the possible effects of EMF from phone masts on a population of White stork (*Ciconia ciconia*). The total productivity in the nests located within 200 m of antennas was 0.86 ± 0.16 versus 1.6 ± 0.14 for those located further than 300 m. Another interesting observation, was that, 40% of the nests within 200 m of the antennae never had any chicks, while only 3.3% located further than 300 m never had chicks.

The influence of a military radar station [75] emitting pulsed modulated microwave radiation of 1200–3000 MHz was examined in tits (*Parus* sp). Experimental nest-boxes

were either exposed to a mean level of 3.41 ± 1.38 or $1.12 \pm 0.84\,W/m^2$. For control nest-boxes the exposure ranged from 0.001 to $0.01\,W/m^2$. No statistically significant differences in the number of eggs or in the number of nestlings were observed between the two series (exposed, control) of tits.

6. Conclusions

The EMF were, are and will be a part of our life. The progress of science will provide the world with new EMF emitting technologies and subsequently with new problems. The monitoring of literature on this scientific field shows a shift of research which follows exactly the new technologies. The era of mobile telephony is beginning.

The evaluation of the possible effects of EMF on the living organism is a complex process that needs the combined contributions of many scientific disciplines. Due to the need for expertise in many different sciences, together with the technical problems of radiation studies, many times the published results are considered deficient in certain aspects. This is inevitable, and not an indication of poor quality. The inability to observe a biological effect in a particular study does not necessarily mean that such effect or/and adverse health effect is not present.

The vertebrate animal studies summarized in the present paper do not suggest strong effects of LF EMF on the male genital system. However, some studies on the development of animals, showed sensitivity, mainly observed in chickens. There is no convincing evidence from studies of mammals (Table 3), that exposure to EMF at levels associated with mobile telecommunications could be harmful for embryonic or postnatal development or for male fertility. On the other hand, the birds appeared to be more sensitive. The effects of EMF on the female genital system need further attention, since two experimental studies cannot lead to definitive conclusions.

The positive findings of the experimental studies with vertebrate animals are mainly attributed to the thermal effects of EMF. No valid evidence was found for the occurrence of non-thermal effects. However the non-thermal mechanisms must be the next target of the research.

The majority of reviewed studies were conducted in laboratories. This fact cannot represent the realistic situation of cell phone communication. On the other hand, the *in vivo* and simultaneously *in situ* studies are very scarce. Only Magras and Xenos conducted an *in situ* experiment which took place near an antenna park. That is because this kind of experiment is very difficult to carry out, and interaction with other exogenous factors could change the results.

One particular deficiency in most studies is that they describe experiments with acute or short-term exposure of animals on EMF. Experiments are needed to perform long-term exposure in order to demonstrate the chronic impact of EMF.

Another point that must be elucidated is that the majority of experimental animals used were small rodents (mice and rats), as well as chicken embryos. Further research is needed with the use of bigger animals such as dog and sheep.

The radiations emitted from masts that are situated in many rural and sylvatic areas could be possibly pathogenic in the wild animals. The wild animal populations could be candidate "experimental material" for closer observation of the possible effects of EMF on vertebrate models.

An important and intriguing aspect of the research is the possible role of the combination of RF with other pollutants such as chemical substances and other forms of radiation, as well as the interaction with drugs.

The potential health effects of EMF should be continually reassessed as new research results become available. EMF exposure guidelines also need to be updated or reconsidered as new scientific information on radiation and health risks is produced. However, additional studies might increase our understanding of the sensitivity of organisms to EMF.

References

[1] J. Juutilainen, Developmental effects of electromagnetic fields, Bioelectromagnetics 7 (2005) S107–S115.
[2] P.A. Valberg, T.E. van Deventer, M.H. Repacholi, Workgroup report: base stations and wireless networks-radiofrequency (RF) exposures and health consequences, Environ. Health Perspect. 115 (2007) 416–424.
[3] M.H. Repacholi, Health risks from the use of mobile phones, Toxicol. Lett. 120 (2001) 323–331.
[4] L.J. Challis, Mechanisms for interaction between RF fields and biological tissue, Bioelectromagnetics 7 (2005) S98–S106.
[5] B.C.A. Windle, On certain early malformations of the embryo, J. Anat. Physiol. 27 (1893) 436–453.
[6] B.C.A. Windle, On the effects of electricity and magnetism on development, J. Anat. Physiol. 29 (1895) 346–351.
[7] H.J. Cook, N.H. Steneck, A.J. Vander, G.L. Kane, Early research on the biological effects of microwave radiation: 1940–1960, Ann. Sci. 37 (1980) 323–351.
[8] W.M. Leach, Genetic, growth and reproductive effects of microwave radiation, Bull. N.Y. Acad. Med. 56 (1980) 249–257.
[9] B. Algers, K. Hennichs, Biological effects of electromagnetic fields. A review, Vet. Res. Commun. 6 (1983) 265–279.
[10] T.E. Bryan, R.P. Gildersleeve, Effects of nonionizing radiation on birds, Comp. Biochem. Physiol. 89A (1988) 511–530.
[11] E. Berman, L. Chacon, D. House, Development of chicken embryos in a pulsed magnetic field, Bioelectromagnetics 11 (1990) 169–187.
[12] J. Juutilainen, Effects of low-frequency magnetic fields on embryonic development and pregnancy, Scand. J. Work Environ. Health. 17 (1991) 149–158.
[13] N. Chernoff, J.M. Rogers, R. Kavet, A review of the literature on potential reproductive and developmental toxicity of electric and magnetic fields, Toxicology 74 (1992) 91–126.
[14] R.L. Brent, W.E. Gordon, W.R. Bennett, D.A. Beckman, Reproductive and teratologic effects of electromagnetic fields, Reprod. Toxicol. 7 (1993) 535–580.
[15] R.P. Jensh, Behavioral teratological studies using microwave radiation: is there an increased risk from exposure to cellular phones and microwave ovens? Reprod. Toxicol. 11 (1997) 601–611.

[16] L. Verschaeve, A. Maes, Genetic, carcinogenic and teratogenic effects of radiofrequency fields, Mutation Res. 410 (1998) 141–165.
[17] H. Huuskonen, M.-L. Lindbohm, J. Juutilainen, Teratogenic and reproductive effects of low-frequency magnetic fields, Mutation Res. 410 (1998) 167–183.
[18] R.L. Brent, Reproductive and teratologic effects of low-frequency electromagnetic fields: a review of *in vivo* and *in vitro* studies using animal models, Teratology 59 (1999) 261–286.
[19] M.E. O'Connor, Mammalian teratogenesis and radiofrequency fields, Proc. IEEE 68 (1980) 56–60.
[20] L.N. Heynick, J.H. Merritt, Radiofrequency fields and teratogenesis, Bioelectromagnetics 6 (2003) (2003) S174–S186.
[21] J. Juutilainen, Developmental effects of extremely low frequency electric and magnetic fields, Radiat. Prot. Dosim. 106 (2003) 385–390.
[22] W. Löscher, Die Auswirkungen electromagnetischer Felder von Mobilfunksendeanlagen auf Leistung, Gesunheit und Verhalten landwirtschaftlicher Nutzitere: Eine Bestandsaufnahme, Der practiche Tierarzt 84 (2003) 850–863.
[23] R.D. Saunders, C.D. McCaig, Developmental effects of physiologically weak electric fields and heat: an overview, Bioelectromagnetics 7 (2005) S127–S132.
[24] K.J. Fernie, S.J. Reynolds, The effects of electromagnetic fields from power lines on avian reproductive biology and physiology: a review, J. Toxic Environ. Health B 8 (2005) 127–140.
[25] D. Krewski, B.W. Glickman, R.W.Y. Habash, B. Habbick, W.G. Lotz, R. Mandeville, F.S. Prato, T. Salem, D.F. Weaver, Recent advances in research on radiofrequency fields and health: 2001–2003, J Toxic Environ. Health B 10 (2007) 287–318.
[26] T. Shigemitsu, K. Yamazaki, S. Nakasono, M. Kakkikawa, A review of studies of the biological effects of electromagnetic fields in the intermediate frequency range, IEEJ Trans. Electr. Electron. Eng. 2 (2007) 405–412.
[27] A. Elbetieha, M.A. Al-Akhras, H. Darmani, Long-term exposure of male and female mice to 50 Hz magnetic field: effects on fertility, Bioelectromagnetics 23 (2002) 168–172.
[28] J.A. Heredia-Rojas, D.E. Caballero-Hernandez, A.O. Rodriguez-De La Fuente, G. Ramos-Alfano, L.E. Rodriguez-Flores, Lack of alterations on meiotic chromosomes and morphological characteristics of male germ cells in mice exposed to a 60 Hz and 2.0 mT magnetic field, Bioelectromagnetics 25 (2004) 63–68.
[29] J.S. Lee, S.S. Ahn, K.C. Jung, Y.W. Kim, S.K. Lee, Effects of 60 Hz electromagnetic field exposure on testicular germ cell apoptosis in mice, Asian J. Androl. 6 (2004) 29–34.
[30] M.K. Chung, S.J. Lee, Y.B. Kim, S.C. Park, D.H. Shin, S.H. Kim, J.C. Kim, Evaluation of spermatogenesis and fertility in F1 male rats after *in utero* and neonatal exposure to extremely low frequency electromagnetic fields, Asian J. Androl. 7 (2005) 189–194.
[31] M.A. Al-Akhras, H. Darmani, A. Elbetieha, Influence of 50 Hz magnetic field on sex hormones and other fertility parameters of adult male rats, Bioelectromagnetics 27 (2006) 127–131.
[32] M.Z. Akdag, S. Dasdag, F. Aksen, B. Isik, F. Yilmaz, Effect of ELF magnetic fields on lipid peroxidation, sperm count, p53 and trace elements, Med. Sci. Monit. 12 (2006) 366–371.
[33] F. Aksen, M.Z. Akdag, A. Ketani, B. Yokus, A. Kaya, S. Dasdag, Effect of 50 Hz 1 mT magnetic field on the uterus and ovaries of rats, Med. Sci. Monit. 12 (2006) 215–220.
[34] S.H. Kim, H.J. Lee, S.Y. Choi, Y.M. Gimm, J.K. Pack, H.D. Choi, Y.S. Lee, Toxicity bioassay in Sprague–Dawley rats exposed to 20 kHz triangular magnetic field for 90 days, Bioelectromagnetics 27 (2006) 105–111.
[35] A.A. Khaki, R.S. Tubbs, M.M. Shoja, J.S. Rad, A. Khaki, R.M. Farahani, S. Zarrintan, T.C. Nag, The effects of an electromagnetic field on the boundary tissue of the seminiferous tubules of the rat: a light and transmission electron microscope study, Folia Morphol. 65 (2006) 188–194.
[36] H.J. Lee, S.H. Kim, S.Y. Choi, Y.M. Gimm, J.K. Pack, H.D. Choi, Y.S. Lee, Long-term exposure of Sprague–Dawley rats to 20 kHz triangular magnetic fields, Int. J. Radiat. Biol. 82 (2006) 285–291.
[37] T.I. Subbotina, O.V. Tereshkina, A.A. Khadartsev, A.A. Yashin, Effect of low-intensity extremely high frequency radiation on reproductive function in Wistar rats, Bull. Exp. Biol. Med. 142 (2006) 189–190.
[38] S. Erpek, M.D. Bilgin, E. Dikicioglu, A. Karul, The effects of low frequency electric field in rat testis, Revue Méd. Vét 158 (2007) 206–212.
[39] S. Dasdag, M.A. Ketani, Z. Akdag, A.R. Ersay, I. Sari, O.C. Demirtas, M.S. Celik, Whole body microwave exposure emitted by cellular phones and testicular function of rats, Urol. Res. 27 (1999) 219–223.
[40] S. Dasdag, M.Z. Akdag, F. Aksen, F. Yilmaz, M. Bashan, M.M. Dasdag, M.S. Celik, Whole body exposure of rats to microwaves emitted from a cell phone does not affect the testes, Bioelectromagnetics 24 (2003) 182–188.
[41] R.J. Aitken, L.E. Bennetts, D. Sawyer, A.M. Wiklendt, B.V. King, Impact of radio frequency electromagnetic radiation on DNA integrity in the male germ line Inter, J. Androl. 28 (2005) 171–179.
[42] M. Ozguner, A. Koyu, G. Cesur, M. Ural, F. Ozguner, A. Gokcimen, N. Delibas, Biological and morphological effects on the reproductive organ of rats after exposure to electromagnetic field, Saudi Med. J. 26 (2005) 405–410.
[43] Z. Forgács, Z. Somosy, G. Kubinyi, J. Bakos, A. Hudák, A. Surján, G. Thuróczy, Effects of whole body 1800 MHz GSM-like microwave exposure on testicular stereidogenesis and histology in mice, Reprod. Toxicol. 22 (2006) 111–117.
[44] E.P. Ribeiro, E.L. Rhoden, M.M. Horn, C. Rhoden, L.P. Lima, L. Toniolo, Effects of sub chronic exposure to radio frequency from a conventional cellular telephone on testicular function in adult rats, J. Urol. 177 (2007) 395–399.
[45] J.G. Yan, M. Agresti, T. Bruce, Y.H. Yan, A. Granlund, H.S. Matloub, Effects of cellular phone emissions on sperm motility in rats, Fertil. Steril. 88 (2007) 957–964.
[46] F. Yilmaz, S. Dasdag, M.Z. Akdag, N. Kilinc, Whole body exposure of radiation emitted from 900 MHz mobile phones does not seem to affect the levels of anti-apoptotic bcl-2 protein, Electromagn. Biol. Med. 27 (2008) 65–72.
[47] S. Dasdag, M.Z. Akdag, E. Ulukaya, A.K. Uzunlar, D. Yegin, Mobile phone exposure does not induce apoptosis on spermatogenesis in rats, Arch. Med. Res. 39 (2008) 40–44.
[48] B. Oral, M. Guney, F. Ozguner, N. Karahan, T. Mungan, S. Comlekci, G. Cesur, Endometrial apoptosis induced by a 900 MHz mobile phone: preventive effects of vitamins E and C, Adv. Ther. 23 (2006) 957–973.
[49] M. Guney, F. Ozguner, B. Oral, N. Karahan, T. Mungan, 900 MHz radiofrequency induced histopathologic changes and oxidative stress in rat endometrium: protection by vitamins E and C, Toxicol. Ind. Health 23 (2007) 411–420.
[50] T. Negishi, S. Imai, M. Itabashi, I. Nishimura, T. Sasano, Studies of 50 Hz circularly polarized magnetic fields of up to 350 mT on reproduction and embryo-fetal development in rats: exposure during organogenesis or during preimplantation, Bioelectromagnetics 23 (2002) 369–389.
[51] Y. Ohnishi, F. Mizuno, T. Sato, M. Yasui, T. Kikuchi, M. Ogawa, Effects of power frequency alternating magnetic fields on reproduction and prenatal development of mice, J. Toxicol. Sci. 27 (2002) 131–138.
[52] Z.E. Gagnon, C. Newkirk, J.A. Conetta, M.A. Sama, S. Sisselman, Teratogenic effect of broad-band electromagnetic field on neonatal mice, J. Environ. Sci. Health A Tox. Hazard Subst. Environ. Eng. 38 (2003) 2465–2481.
[53] M.K. Chung, J.C. Kim, S.H. Myung, D.I. Lee, Developmental toxicity evaluation of ELF magnetic fields in Sprague–Dawley rats, Bioelectromagnetics 24 (2003) 231–240.
[54] M.S. Lahijani, K. Sajadi, Development of preincubated chicken eggs following exposure to 50 Hz electromagnetic fields with 1.33–7.32 mT flux densities, Indian J. Exp. Biol. 42 (2004) 858–865.
[55] S.H. Kim, J.E. Song, S.R. Kim, H. Oh, Y.M. Gimm, D.S. Yoo, J.K. Pack, Y.S. Lee, Teratological studies of prenatal exposure of mice to a

20 kHz sawtooth magnetic field, Bioelectromagnetics 25 (2004) 114–117.

[56] O. Roda-Murillo, J.A. Roda-Moreno, M.T. Morente–Chiquero, Effects of low-frequency magnetic fields on different parameters of embryo of *Gallus domesticus*, Electromagn. Biol. Med. 24 (2005) 55–62.

[57] K. Saito, H. Suzuki, K. Suzuki, Teratogenic effects of static magnetic field on mouse fetuses, Reprod. Toxicol. 22 (2006) 118–124.

[58] Y.N. Cao, Y. Zhang, Y. Liu, Effects of exposure to extremely low frequency electromagnetic fields on reproduction of female mice and development of offspring, Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi 24 (2006) 468–470.

[59] M.S. Lahijani, S.E. Nojooshi, S.F. Siadat, Light and electron microscope studies of effects of 50 Hz electromagnetic fields on preincubated chick embryo, Electromagn. Biol. Med. 26 (2007) 83–98.

[60] W.F. Krueger, A.J. Giarola, J.W. Bradley, A. Shrekenhamer, Effects of electromagnetic fields on fecundity in the chicken, Ann. N.Y. Acad. Sci. 247 (1975) 391–400.

[61] R.P. Jensh, I. Weinberg, R.I. Brent, Teratologic studies of prenatal exposure of rats to 915 MHz microwave radiation, Radiat. Res. 92 (1982) 160–171.

[62] R.P. Jensh, W.H. Vogel, R.I. Brent, Postnatal functional analysis of prenatal exposure of rats to 915 MHz microwave radiation, Int. J. Toxicol. 1 (1982) 73–90.

[63] E. Berman, C. Weil, P.A. Philips, H.B. Carter, D.E. House, Fetal and maternal effects of continual exposure of rats to 970 MHz circularly-polarized microwaves, Electromagn. Biol. Med. 11 (1992) 43–54.

[64] S. Klug, M. Hetscher, S. Giles, S. Kohlsman, K. Kramer, The lack of effects of nonthermal RF electromagnetic fields on the development of rat embryos grown in culture, Life Sci. 61 (1997) 1789–1802.

[65] I.N. Magras, T.D. Xenos, RF radiation-induced changes in the prenatal development of mice, Bioelectromagnetics 18 (1997) 455–461.

[66] M. Bornhausen, H. Scheingraber, Prenatal exposure to 900 MHz cell phone electromagnetic fields had no effect on operant-behaviour performances of adult rats, Bioelectromagnetics 21 (2000) 566–574.

[67] S. Dasdag, M.Z. Akdag, O. Ayyildiz, O.C. Demirtas, M. Yayla, C. Sert, Do cellular phones alter blood parameters and birth weight of rats? Electromagn. Biol. Med. 19 (2000) 107–113.

[68] B.L. Cobb, J.R. Jauchem, P.A. Mason, M.P. Dooley, S.A. Miller, J.M. Ziriax, M.R. Murphy, Neural and behavioural teratological evaluation of rats exposed to Ultra-Wideband electromagnetic fields, Bioelectromagnetics 21 (2000) 524–537.

[69] M. Bastide, B.J. Youbicier-Simoa, J.C. Lebecq, J. Giaimis, Toxicologic study of electromagnetic radiation emitted by television and video display screens and cellular telephones on chickens and mice, Indoor Built Environ. 10 (2001) 291–298.

[70] Y. Grigoryev, Biological effects of mobile phone electromagnetic field on chick embryo (Risk assessment using the mortality rate), Radiats. Biol. Radioecol. 43 (2003) 541–543.

[71] I.V. Ingole, S.K. Ghosh, Cell phone radiation and developing tissues in chicken embryo—a light microscopic study of kidneys, J. Anat. Soc. India 55 (2006) 19–23.

[72] T. Kumlin, H. Iivonen, P. Miettenen, A. Junoven, T. van Groen, L. Puranen, R. Pitkäaho, R. Juutilainen, H. Tanila, Mobile phone radiation and the developing brain: behavioral and morphological effects in juvenile rats, Radiat. Res. 168 (2007) 471–479.

[73] F. Batellier, I. Couty, D. Picard, J.P. Brillard, Effects of exposing chicken eggs to a cell phone in 'call' position over the entire incubation period, Theriogenology 69 (2008) 737–745.

[74] A. Balmori, Possible effects of electromagnetic fields from phone masts on a population of White stork (*Ciconia ciconia*), Electromagn. Biol. Med. 24 (2005) 109–119.

[75] L. Rejt, T. Mazgajski, R. Kubacki, J. Kieliszek, E. Sobiczewska, S. Szmigielski, Influence of radar radiation on breeding biology of tits (*Parus* sp), Electromagn. Biol. Med. 26 (2007) 235–238.

ELSEVIER

Pathophysiology 16 (2009) 191–199

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Electromagnetic pollution from phone masts. Effects on wildlife

Alfonso Balmori

Direccion General del Medio Natural, Consejería de Medio Ambiente, Junta de Castilla y Leon, C/Rigoberto Cortejoso, 14, 47014 Valladolid, Spain

Received 10 August 2008; received in revised form 28 August 2008; accepted 30 January 2009

Abstract

A review on the impact of radiofrequency radiation from wireless telecommunications on wildlife is presented. Electromagnetic radiation is a form of environmental pollution which may hurt wildlife. Phone masts located in their living areas are irradiating continuously some species that could suffer long-term effects, like reduction of their natural defenses, deterioration of their health, problems in reproduction and reduction of their useful territory through habitat deterioration. Electromagnetic radiation can exert an aversive behavioral response in rats, bats and birds such as sparrows. Therefore microwave and radiofrequency pollution constitutes a potential cause for the decline of animal populations and deterioration of health of plants living near phone masts. To measure these effects urgent specific studies are necessary.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Effects on wildlife; Effects on birds; Electromagnetic radiation; Mammals; Microwaves; Mobile telecommunications; Non-thermal effects; Phone masts; Radiofrequencies

1. Introduction

Life has evolved under the influence of two omnipresent forces: gravity and electromagnetism. It should be expected that both play important roles in the functional activities of organisms [1]. Before the 1990's radiofrequencies were mainly from a few radio and television transmitters, located in remote areas and/or very high places. Since the introduction of wireless telecommunication in the 1990's the rollout of phone networks has caused a massive increase in electromagnetic pollution in cities and the countryside [2,3].

Multiple sources of mobile communication result in chronic exposure of a significant part of the wildlife (and man) to microwaves at non-thermal levels [4]. In recent years, wildlife has been chronically exposed to microwaves and RFR (Radiofrequency radiation) signals from various sources, including GSM and UMTS/3G wireless phones and base stations, WLAN (Wireless Local Area Networks), WPAN (Wireless Personal Area Networks such as Bluetooth), and DECT (Digital Enhanced (former European) Cordless Telecommunications) that are erected indiscriminately without studies of environmental impact measuring long-term effects. These exposures are characterized by low intensities, varieties of signals, and long-term durations. The greater portion of this exposure is from mobile telecommunications (geometric mean in Vienna: 73% [5]). In Germany the GSM cellular phone tower radiation is the dominating high frequency source in residential areas [6]. Also GSM is the dominating high frequency source in the wilderness of Spain (personal observation).

Numerous experimental data have provided strong evidence of athermal microwave effects and have also indicated several regularities in these effects: dependence of frequency within specific frequency windows of "resonance-type"; dependence on modulation and polarization; dependence on intensity within specific intensity windows, including super-low power density comparable with intensities from base stations/masts [4,7–9]. Some studies have demonstrated different microwave effects depending on wavelength in the range of mm, cm or m [10,11]. Duration of exposure may be as important as power density. Biological effects resulting from electromagnetic field radiation might depend on dose, which indicates long-term accumulative effects [3,9,12]. Modulated and pulsed radiofrequencies seem to be more effective in producing effects [4,9]. Pulsed waves (in blasts), as well as certain low frequency modulations exert greater

E-mail addresses: abalmori@ono.com, balmaral@jcyl.es.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.007

biological activity [11,13–15]. This observation is important because cell phone radiation is pulsed microwave radiation modulated at low frequencies [8,9].

Most of the attention on possible biological effects of electromagnetic radiation from phone masts has been focused on human health [5,16–21]. The effects of electromagnetic pollution on wildlife, have scarcely been studied [22–25].

The objective of this review is to detail advances in knowledge of radiofrequencies and microwave effects on wildlife. Future research may help provide a better understanding of electromagnetic field (EMF) effects on wildlife and plants and their conservation.

2. Effects on exposed wildlife

2.1. Effects on birds

2.1.1. Effects of phone mast microwaves on white stork

In monitoring a white stork (*Ciconia ciconia*) population in Valladolid (Spain) in vicinity of Cellular Phone Base Stations, the total productivity in nests located within 200 m of antennae, was 0.86 ± 0.16. For those located further than 300 m, the result was practically doubled, with an average of 1.6 ± 0.14. Very significant differences among total productivity were found ($U = 240$; $P = 0.001$, Mann–Whitney test). Twelve nests (40%) located within 200 m of antennae never had chicks, while only one (3.3%) located further than 300 m had no chicks. The electric field intensity was higher on nests within 200 m (2.36 ± 0.82 V/m) than nests further than 300 m (0.53 ± 0.82 V/m). In nesting sites located within 100 m of one or several cellsite antennae with the main beam of radiation impacting directly (Electric field intensity >2 V/m) many young died from unknown causes. Couples frequently fought over nest construction sticks and failed to advance the construction of the nests. Some nests were never completed and the storks remained passively in front of cellsite antennae. These results indicate the possibility that microwaves are interfering with the reproduction of white stork [23]. (Fig. 1)

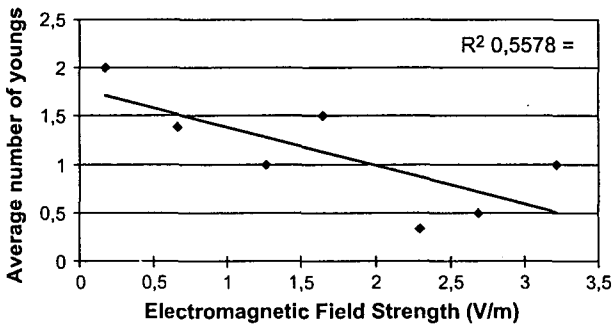


Fig. 1. Average number of youngs and electric field intensity (V/m) in 60 nests of white storks (*Ciconia ciconia*) (Hallberg, Ö with data of Balmori, 2005 [23]).

2.1.2. Effects of phone mast microwaves on house sparrows

A possible effect of long-term exposure to low-intensity electromagnetic radiation from mobile phone (GSM) base stations on the number of house sparrows during the breeding season was studied in Belgium. The study was carried out sampling 150 point locations within six areas to examine small-scale geographic variation in the number of house sparrow males and the strength of electromagnetic radiation from base stations. Spatial variation in the number of house sparrow males was negative and highly significantly related to the strength of electric fields from both the 900 and 1800 MHz downlink frequency bands and from the sum of these bands (Chi-square-tests and AIC-criteria, $P < 0.001$). This negative relationship was highly similar within each of the six study areas, despite differences among areas in both the number of birds and radiation levels. Fewer house sparrow males were seen at locations with relatively high electric field strength values of GSM base stations and therefore support the notion that long-term exposure to higher levels of radiation negatively affects the abundance or behavior of house sparrows in the wild [24].

In another study with point transect sampling performed at 30 points visited 40 times in Valladolid (Spain) between 2002 and 2006, counting the sparrows and measuring the mean electric field strength (radiofrequencies and microwaves: 1 MHz to 3 GHz range). Significant declines ($P = 0.0037$) were observed in mean bird density over time, and significantly low bird density was observed in areas with high electric field strength. The logarithmic regression of the mean bird density vs. field strength groups (considering field strength in 0.1 V/m increments) was $R = -0.87$; $P = 0.0001$ According to this calculation, no sparrows would be expected to be found in an area with field strength >4 V/m [25]. (Fig. 2)

In the United Kingdom a decline of several species of urban birds, especially sparrows, has recently happened [26]. The sparrow population in England has decreased in the last 30 years from 24 million to less than 14. The more abrupt decline, with 75% descent has taken place from 1994 to 2002. In 2002, the house sparrow was added to the Red List of U.K. endangered species [27]. This coincides with the rollout of mobile telephony and the

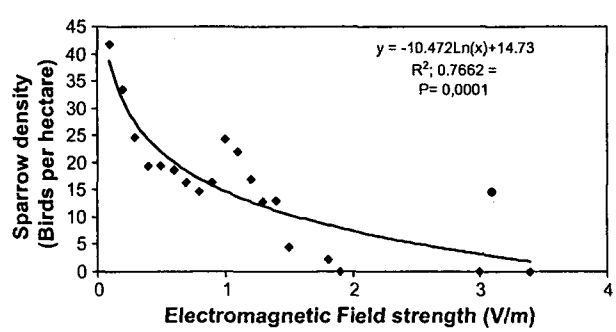


Fig. 2. Mean sparrow density as a function of electric field strength grouped in 0.1 V/m. (Balmori and Hallberg, 2007 [25]).

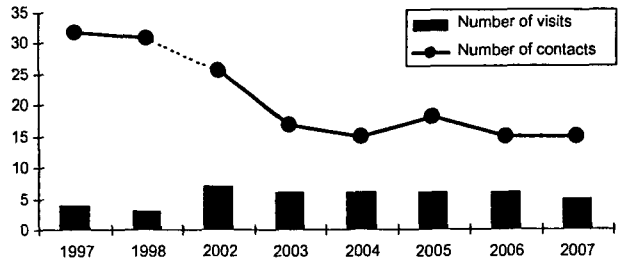


Fig. 3. Annual number of contacts (Mean) for 14 species studied in "Campo Grande" urban park (lack the information of the years 1999–2001).

possible relationship of both circumstances should be investigated.

In Brussels, many sparrows have disappeared recently [28]; similar declines have been reported in Dublin [29]. Van der Poel (cited in Ref. [27]) suggested that sparrows might be declining in Dutch urban centres also.

2.1.3. *Effects on the bird community at an urban park*

Microwaves may be affecting bird populations in places with high electromagnetic pollution. Since several antennas were installed in proximities of "Campo Grande" urban park (Valladolid, Spain) the bird population has decreased and a reduction of the species and breeding couples has occurred. Between 1997 and 2007, of 14 species, 3 species have disappeared, 4 are in decline and 7 stay stable (Balmori, unpublished data) (Fig. 3). In this time the air pollution (SO2, NO2, CO and Benzene) has diminished.

During the research some areas called "silence areas" contaminated with high microwave radiation (>2 V/m), where previously different couples usually bred and later disappeared, have been found. Several anomalies in magpies (*Pica pica*) were detected: plumage deterioration, locomotive problems (limps and deformations in the paws), partial albinism and melanism, especially in flanks [30]. Recently cities have increased cases of partial albinism and melanism in birds (*Passer domesticus*, *Turdus merula* and *P. pica*) (personal observation).

2.1.4. *Possible physiological mechanisms of the effects found in birds*

Current scientific evidence indicates that prolonged exposure to EMFs, at levels that can be encountered in the environment, may affect immune system function by affecting biological processes [3,31,32]. A stressed immune system may increase the susceptibility of a bird to infectious diseases, bacteria, viruses, and parasites [33].

The plumage of the birds exposed to microwaves looked, in general, discolorated and lack of shine. This not only occurred in ornamental birds; such as peacocks, but also in wild birds; such as, tits, great tits, house sparrows, etc (personal observation). We must mention that plumage deterioration is the first sign of weakening or illnesses in birds since damaged feathers are a sure sign of stress.

Physiological conditions during exposure minimize microwave effects. Radical scavengers/antioxidants might be involved in effects of microwaves [4].

Microwaves used in cellphones produce an athermal response in several types of neurons of the birds nervous system [34]. Several studies addressed behavior and teratology in young birds exposed to electromagnetic fields [23,25,35–37]. Most studies indicate that electromagnetic field exposure of birds generally changes, but not always consistently in effect or in direction, their behavior, reproductive success, growth and development, physiology and endocrinology, and oxidative stress [37]. These results can be explained by electromagnetic fields affecting the birds' response to the photoperiod as indicated by altered melatonin levels [38].

Prolonged mobile phone exposure may have negative effects on sperm motility characteristics and male fertility as has been demonstrated in many studies made in man and rats [39–46]. EMF and microwaves can affect reproductive success in birds [23,25,35,36,47]. EMF exposure affected reproductive success of kestrels (*Falco sparverius*), increasing fertility, egg size, embryonic development and fledging success but reducing hatching success [35,36].

The radiofrequency and microwaves from mobile telephony can cause genotoxic effects [48–55]. Increases in cytological abnormalities imply long-term detrimental effects since chromosomal damage is a mechanism relevant to causation of birth defects and cancer [55].

Long-term continuous, or daily repeated EMF exposure can induce cellular stress responses at non-thermal power levels that lead to an accumulation of DNA errors and to inhibition of cell apoptosis and cause increased permeability of blood–brain barrier due to stabilization of endothelial cell stress fibers. Repeated occurrence of these events over a long period of time (years) could become a health hazard due to a possible accumulation of brain tissue damage. These findings have important implications with regards to potential dangers from prolonged and repeated exposure to non-ionizing radiation [56,57].

Pulsed magnetic fields can have a significant influence on the development and incidence of abnormalities in chicken embryos. In five of six laboratories, exposed embryos exhibited more structural anomalies than controls. If the data from all six laboratories are pooled, the difference for the incidence of abnormalities in exposed embryos and controls is highly significant [58]. Malformations in the nervous system and heart, and delayed embryo growth are observed. The embryo is most sensitive to exposure in the first 24 h of incubation [58]. An increase in the mortality [59] and appearance of morphological abnormalities, especially of the neural tube [13,60,61] has been recorded in chicken embryos exposed to pulsed magnetic fields, with different susceptibility among individuals probably for genetic reasons. A statistically significant high mortality rate of chicken embryos subjected to radiation from a cellphone, compared to the control group exists [62,63]. In another study eggs exposed to a magnetic

field intensity of 0.07 T showed embryonic mortality during their incubation was higher. The negative effect of the magnetic field was manifested also by a lower weight of the hatched chicken [64]. Bioelectric fields have long been suspected to play a causal role in embryonic development. Alteration of the electrical field may disrupt the chemical gradient and signals received by embryo cells. It appears that in some manner, cells sense their position in an electrical field and respond appropriately. The disruption of this field alters their response. Endogenous current patterns are often correlated with specific morphogenetic events [65].

Available data suggests dependencies of genotype, gender, physiological and individual factors on athermal microwave effects [4,9]. Genomic differences can influence cellular responses to GSM Microwaves. Data analysis has highlighted a wide inter-individual variability in response, which was replicated in further experiments [4]. It is possible that each species and each individual, show different susceptibility to radiation, since vulnerability depends on genetic tendency, and physiologic and neurological state of the irradiated organism [15,35–37,61,66–68]. Different susceptibility of each species has also been proven in wild birds exposed to electromagnetic fields from high-voltage power lines [47].

2.2. *Effects on mammals*

2.2.1. *Alarm and aversion behavior*

Rats spent more time in the halves of shuttle boxes that were shielded from 1.2 GHz. Microwaves irradiation. The average power density was about 0.6 mW/cm^2. Data revealed that rats avoided the pulsed energy, but not the continuous energy, and less than 0.4 mW/cm^2 average power density was needed to produce aversion [69]. Navakatikian & Tomashevskaya [70] described a complex series of experiments in which they observed disruption of rat behavior (active avoidance) from radiofrequency radiation. Behavioral disruption was observed at a power density as low as 0.1 mW/cm^2 (0.027 W/kg). Mice in an experimental group exposed to microwave radiation expressed visible individual panic reaction, disorientation and a greater degree of anxiety. In the sham exposed group these deviations of behavior were not seen and all animals show collective defense reaction [71]. Microwave radiation at 1.5 GHz pulsing 16 ms. At 0.3 mW/cm^2 power density, in sessions of 30 min/day over one month produced anxiety and alarm in rabbits [72].

Electromagnetic radiation can exert an aversive behavioral response in bats. Bat activity is significantly reduced in habitats exposed to an electromagnetic field strength greater than 2 V/m [73]. During a study in a free-tailed bat colony (*Tadarida teniotis*) the number of bats decreased when several phone masts were placed 80 m from the colony [74].

2.2.2. *Deterioration of health*

Animals exposed to electromagnetic fields can suffer a deterioration of health and changes in behavior [75,76].

There was proof of frequent death in domestic animals; such as, hamsters and guinea pigs, living near mobile telecommunication base stations (personal observation).

The mice in an experimental group exposed to microwave radiation showed less weight gain compared to control, after two months. The amount of food used was similar in both groups [71]. A link between electromagnetic field exposure and higher levels of oxidative stress appears to be a major contributor to aging, neurodegenerative diseases, immune system disorders, and cancer in mammals [33].

The effects from GSM base transceiver station (BTS) frequency of 945 MHz on oxidative stress in rats were investigated. When EMF at a power density of 3.67 W/m^2, below current exposure limits, were applied, MDA (malondialdehyde) level was found to increase and GSH (reduced glutathione) concentration was found to decrease significantly ($P < 0.0001$). Additionally, there was a less significant ($P = 0.0190$) increase in SOD (superoxide dismutase) activity under EM exposure [77].

2.2.3. *Problems in reproduction*

In the town of Casavieja (Ávila, Spain) a telephony antenna was installed that had been in operation for about 5 years. Then some farmers began blaming the antenna for miscarriages in many pigs, 50–100 m from the antenna (on the outskirts of the town). Finally the topic became so bad that the town council decided to disassemble the antenna. It was removed in the spring 2005. From this moment onwards the problems stopped (C. Lumbreras personal communication).

A Greek study reports a progressive drop in the number of rodent births exposed to radiofrequencies. The mice exposed to 0.168 μW/cm^2 become sterile after five generations, while those exposed to 1.053 μW/cm^2 became sterile after only three generations [22].

In pregnant rats exposed to 27.12 MHz continuous waves at 100 μW/cm^2 during different periods of pregnancy, half the pregnancies miscarried before the twentieth day of gestation, compared to only a 6% miscarriage rate in unexposed controls, and 38% of the viable foetuses had incomplete cranial ossification, compared to less than 6% of the controls. Findings included a considerable increase in the percentage of total reabsorptions (post-implantation losses consequent to RF radiation exposure in the first post-implantation stage). Reduced body weight in the exposed dams reflected a negative influence on their health. It seems that the irradiation time plays an important role in inducing specific effects consequent to radiofrequency radiation exposure [78]. There was also a change in the sex ratio, with more males born to rats that had been irradiated from the time of conception [2]. Moorhouse and Macdonald [79] find a substantial decline in female Water Vole numbers in the radio-collared population, apparently resulting from a male skew in the sex ratios of offspring born to this population. Recruits to the *radio-tracked* population were skewed heavily in favour of males (43:13). This suggests that radio-collaring of females caused male-skewed sex ratios.

Mobile phone exposure may have negative effects on sperm motility characteristics and male fertility in rats [46]. Other studies find a decrease of fertility, increase of deaths after birth and dystrophic changes in their reproductive organs [11]. Intermittent exposure showed a stronger effect than continuous exposure [4]. Brief, intermittent exposure to low-frequency EM fields during the critical prenatal period for neurobehavioral sex differentiation can demasculinize male scent marking behavior and increase accessory sex organ weights in adulthood [80].

In humans, magnetic field exposures above 2.0 mG were positively associated with miscarriage risk [81]. Exposure of pregnant women to mobile phone significantly increased foetal and neonatal heart rate, and significantly decreased the cardiac output [82].

2.2.4. Nervous system

Microwaves may affect the blood brain barrier which lets toxic substances pass through from the blood to the brain [83]. Adang et al. [84] examined the effect of microwave exposure to a GSM-like frequency of 970 MHz pulsed waves on the memory in rats by means of an object recognition task. The rats that have been exposed for 2 months show normal exploratory behavior. The animals that have been exposed for 15 months show derogatory behavior. They do not make the distinction between a familiar and an unfamiliar object. In the area that received radiation directly from "Location Skrunda Radio Station" (Latvia), exposed children had less developed memory and attention, their reaction time was slower and neuromuscular apparatus endurance was decreased [85]. Exposure to cell phones prenatally and, to a lesser degree, postnatally was associated with behavioral difficulties such as emotional and hyperactivity problems around 7 years of age [86]. Electromagnetic radiation caused modification of sleep and alteration of cerebral electric response (EEG) [87–89]. Microwave radiation from phone masts may cause aggressiveness in people and animals (personal observation).

2.3. Effects on amphibians

Disappearance of amphibians and other organisms is part of the global biodiversity crisis. An associated phenomenon is the appearance of large numbers of deformed amphibians. The problem has become more prevalent, with deformity rates up to 25% in some populations, which is significantly higher than previous decades [90]. Balmori [91] proposed that electromagnetic pollution (in the microwave and radiofrequency range) is a possible cause for deformations and decline of some wild amphibian populations.

Two species of amphibians were exposed to magnetic fields at various stages of development. A brief treatment of early amphibian embryos produced several types of abnormalities [92]. Exposure to a pulsed electromagnetic field produced abnormal limb regeneration in adult Newts [93]. Frog tadpoles (*Rana temporaria*) developed under electromagnetic field (50 Hz, 260 A/m) have increased mortality. Exposed tadpoles developed more slowly and less synchronously than control tadpoles and remain at the early stages for longer. Tadpoles developed allergies and EMF caused changes in blood counts [94].

In a current study exposing eggs and tadpoles ($n = 70$) of common frog (*R. temporaria*) for two months, from the phase of eggs until an advanced phase of tadpole, to four telephone base stations located 140 m away: with GSM system 948.0–959.8 MHz; DCS system: 1830.2–1854.8; 1855.2–1879.8 MHz. and UMTS system: 1905–1910; 1950–1965; 2140–2155 MHz. (electric field intensity: 1.847–2.254 V/m). A low coordination of movements, an asynchronous growth, with big and small tadpoles, and a high mortality (90%) was observed. The control group ($n = 70$), under the same conditions but inside a Faraday cage (metallic shielding component: EMC-reinforcement fabrics 97442 Marburg Technic), the coordination of movements was normal, the development was synchronously and the mortality rate was only 4.2% [95].

2.4. Effects on insects

The microwaves may affect the insects. Insects are the basis and key species of ecosystems and they are especially sensitive to electromagnetic radiation that poses a threat to nature [96].

Carpenter and Livstone [97] irradiated pupae of Tenebrio molitor with 10 GHz microwaves at 80 mW for 20–30 min and 20 mW for 120 min obtained a rise in the proportion of insects with abnormalities or dead. In another study exposing fruit flies (*Drosophila melanogaster*) to mobile phone radiation, elevated stress protein levels (Hsp70) was obtained, which usually means that cells are exposed to adverse environmental conditions ('non-thermal shock') [98]. Panagopoulos et al. [99] exposed fruit flies (*D. melanogaster*) to radiation from a mobile phone (900 MHz) during the 2–5 first days of adulthood. The reproductive capacity of the species reduced by 50–60% in modulated radiation conditions (emission while talking on the phone) and 15–20% with radiation nomodulated (with the phone silent). The results of this study indicate that this radiation affects the gonadal development of insects in an athermal way. The authors concluded that radio frequencies, specifically GSM, are highly bioactive and provoke significant changes in physiological functions of living organisms. Panagopoulos et al. [100] compare the biological activity between the two systems GSM 900 MHz and DCS 1800 MHz in the reproductive capacity of fruit flies. Both types of radiation were found to decrease significantly and non-thermally the insect's reproductive capacity, but GSM 900 MHz seems to be even more bioactive than DCS 1800 MHz. The difference seems to be dependent mostly on field intensity and less on carrier frequency.

A study in South Africa finds a strong correlation between decrease in ant and beetle diversity with the

electromagnetic radiation exposure (D. MacFadyen, personal communication.). A decrease of insects and arachnids near base stations was detected and corroborated by engineers and antenna's maintenance staff [101]. In houses near antennas an absence of flies, even in summer, was found.

In a recent study carried out with bees in Germany, only a few bees irradiated with DECT radiation returned to the beehive and they needed more time. The honeycomb weight was lower in irradiated bees [102]. In recent years a "colony collapse disorder" is occurring that some authors relate with pesticides and with increasing electromagnetic pollution [96].

The disappearance of insects could have an influence on bird's weakening caused by a lack of food, especially at the first stages in a young bird's life.

2.5. *Effects on trees and plants*

The microwaves may affect vegetables. In the area that received radiation directly from "Location Skrunda Radio Station" (Latvia), pines (*Pinus sylvestris*) experienced a lower growth radio. This did not occur beyond the area of impact of electromagnetic waves. A statistically significant negative correlation between increase tree growth and intensity of electromagnetic field was found, and was confirmed that the beginning of this growth decline coincided in time with the start of radar emissions. Authors evaluated other possible environmental factors which might have intervened, but none had noticeable effects [103]. In another study investigating cell ultrastructure of pine needles irradiated by the same radar, there was an increase of resin production, and was interpreted as an effect of stress caused by radiation, which would explain the aging and declining growth and viability of trees subjected to pulsed microwaves. They also found a low germination of seeds of pine trees more exposed [104]. The effects of Latvian radar was also felt by aquatic plants. *Spirodela polyrrhiza* exposed to a power density between 0.1 and 1.8 $\mu W/cm^2$ had lower longevity, problems in reproduction and morphological and developmental abnormalities compared with a control group who grew up far from the radar [105].

Chlorophylls were quantitatively studied in leaves of black locust (*Robinia pseudoacacia* L.) seedlings exposed to high frequency electromagnetic fields of 400 MHz. It was revealed that the ratio of the two main types of chlorophyll was decreasing logarithmically to the increase of daily exposure time [106].

Exposed tomato plants (*Lycopersicon esculentum*) to low level (900 MHz, 5 V/m) electromagnetic fields for a short period (10 min) measured changes in abundance of three specific mRNA after exposure, strongly suggesting that they are the direct consequence of application of radio-frequency fields and their similarities to wound responses suggests that this radiation is perceived by plants as an injurious stimulus [107]. Non-thermal exposure to radiofrequency fields induced oxidative stress in duckweed (*Lemna minor*) as well as unespecific stress responses, especially of antioxidative enzymes [108].

For some years progressive deterioration of trees near phone masts have been observed in Valladolid (Spain). Trees located inside the main lobe (beam), look sad and feeble, possibly slow growth and a high susceptibility to illnesses and plagues. In places we have measured higher electric field intensity levels of radiation (>2 V/m) the trees show a more notable deterioration [109]. The tops of trees are dried up where the main beams are directed to, and they seem to be most vulnerable if they have their roots close to water. The trees don't grow above the height of the other ones and, those that stand out far above, have dried tops (Hargreaves, personal communication and personal observation). White and black poplars (*Populus sp.*) and willows (*Salix sp.*) are more sensitive. There may be a special sensitivity of this family exists or it could be due to their ecological characteristics forcing them to live near water, and thus electric conductivity. Other species as *Platanus sp.* and *Lygustrum japonicum,* are more resistant (personal observation). Schorpp [110] presents abundant pictures and explanations of what happens to irradiated trees.

3. Conclusions

This literature review shows that pulsed telephony microwave radiation can produce effects especially on nervous, cardiovascular, immune and reproductive systems [111]:

- Damage to the nervous system by altering electroencephalogram, changes in neural response or changes of the blood–brain barrier.
- Disruption of circadian rhythms (sleep–wake) by interfering with the pineal gland and hormonal imbalances.
- Changes in heart rate and blood pressure.
- Impairment of health and immunity towards pathogens, weakness, exhaustion, deterioration of plumage and growth problems.
- Problems in building the nest or impaired fertility, number of eggs, embryonic development, hatching percentage and survival of chickens.
- Genetic and developmental problems: problems of locomotion, partial albinism and melanism or promotion of tumors.

In the light of current knowledge there is enough evidence of serious effects from this technology to wildlife. For this reason precautionary measures should be developed, alongside environmental impact assessments prior to installation, and a ban on installation of phone masts in protected natural areas and in places where endangered species are present. Surveys should take place to objectively assess the severity of effects.

Acknowledgment

The author is grateful to Denise Ward and Örjan Hallberg.

References

[1] J.M.R. Delgado, Biological effects of extremely low frequency electromagnetic fields, J. Bioelectr. 4 (1985) 75–91.
[2] A. Firstenberg, Microwaving Our Planet: The Environmental Impact of the Wireless Revolution, 11210, Cellular Phone Taskforce, Brooklyn, NY, 1997.
[3] A.L. Galeev, The effects of microwave radiation from mobile telephones on humans and animals, Neurosci. Behav. Physiol. 30 (2000) 187–194.
[4] I. Belyaev, Non-thermal biological effects of microwaves, Microw. Rev. 11 (2005) 13–29, http://www.mwr.medianis.net/pdf/Vol11No2-03-IBelyaev.pdf.
[5] H.P. Hutter, H. Moshammer, P. Wallner, M. Kundi, Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations, Occup. Environ. Med. 63 (2006) 307–313.
[6] T. Haumann, U. Munzenberg, W. Maes, P. Sierck, HF-radiation levels of GSM cellular phone towers in residential areas, in: 2nd International Workshop on Biological effects of EMFS, Rhodes, Greece, 2002.
[7] W.R. Adey, Tissue interactions with non-ionizing electromagnetic fields, Physiol. Rev. 61 (1981) 435–514.
[8] G.J. Hyland, Physics and biology of mobile telephony, Lancet 356 (2000) 1–8.
[9] H. Lai, Biological effects of radiofrequency electromagnetic field, in: Encyclopaedia of Biomaterials and Biomedical Engineering, 2005, doi:10.1081/E-EBBE-120041846, pp. 1–8.
[10] S. Kemerov, M. Marinkev, D. Getova, Effects of low-intensity electromagnetic fields on behavioral activity of rats, Folia Med. 41 (1999) 75–80.
[11] N. Nikolaevich, A. Igorevna, and G. Vasil, Influence of high-frequency electromagnetic radiation at non-thermal intensities on the human body (A review of work by Russian and Ukrainian researchers), No place to hide, 3 (Supplement), 2001.
[12] W.R. Adey, Bioeffects of mobile communications fields: possible mechanisms for cumulative dose. in: N. Kuster, Q. Balzano, J.C. Lin, (Eds.), Mobile communications safety, New York: Chapman & Hall, 1997, pp. 95–131.
[13] A. Úbeda, M.A. Trillo, L. Chacón, M.J. Blanco, J. Leal, Chick embryo development can be irreversibly altered by early exposure to weak extremely-low-frequency magnetic fields, Bioelectromagnetics 15 (1994) 385–398.
[14] I.U.G. Grigoriev, Role of modulation in biological effects of electromagnetic radiation, Radiats. Biol. Radioecol. 36 (1996) 659–670.
[15] G.J. Hyland, The physiological and environmental effects of non-ionising electromagnetic radiation, Working document for the STOA Panel, European Parliament, Directorate General for Research, 2001.
[16] R. Santini, J.M. Santini, P. danze, M. Leruz, M. Seigne, Enquête sur la santé de riverains de stations relais: I. Incidences de la distance et du sexe, Pathol. Biol. 50 (2002) 369–373.
[17] R. Santini, P. Santini, J.M. Le Ruz, M. Danze, M. Seigne, Survey study of people living in the vicinity of cellular phone base stations, Electromagn. Biol. Med. 22 (2003) 41–49.
[18] R. Santini, P. Santini, J.M. Danze, P. Le Ruz, M. Seigne, Symptoms experienced by people in vicinity of base stations: II/Incidences of age, duration of exposure, location of subjects in relation to the antennas and other electromagnetic factors, Pathol. Biol. 51 (2003) 412–415.
[19] E.A. Navarro, J. Segura, M. Portolés, C. Gómez Perretta, The microwave syndrome: a preliminary study in Spain, Electromagn. Biol. Med. 22 (2003) 161–169.
[20] G. Oberfeld, E. Navarro, M. Portoles, C. Maestu, C. Gomez-Perretta, The microwave syndrome—further aspects of a Spanish study, in: EBEA Congres Kos, Greece, 2004.
[21] G. Abdel-Rassoul, M.A. Salem, A. Michael, F. Farahat, M. El-Batanouny, E. Salem, Neurobehavioral effects among inhabitants around mobile phone base stations, Neurotoxicology 28 (2007) 434–440.
[22] I.N. Magras, T.D. Xenos, Radiation-induced changes in the prenatal development of mice, Bioelectromagnetics 18 (1997) 455–461.
[23] A. Balmori, Possible effects of electromagnetic fields from phone masts on a population of white stork (*Ciconia ciconia*), Electromagn. Biol. Med. 24 (2005) 109–119.
[24] J. Everaert, D. Bauwens, A possible effect of electromagnetic radiation from mobile phone base stations on the number of breeding House Sparrows (*Passer domesticus*), Electromagn. Biol. Med. 26 (2007) 63–72.
[25] A. Balmori, Ö. Hallberg, The urban decline of the house sparrow (*Passer domesticus*): a possible link with electromagnetic radiation, Electromagn. Biol. Med. 26 (2007) 141–151.
[26] M.J. Raven, D.G. Noble, S.R. Baillie, The breeding bird survey (2002), BTO Research Report 334, British Trust for Ornithology, Thetford, 2003.
[27] J.D. Summers-Smith, The decline of the house sparrow: a review, Brit. Birds 96 (2003) 439–446.
[28] J. De Laet, Ligue Royale Belgue pour la Protection des Oiseaux avec l'Université de Gand, 2004, <http://www.protectiondesoiseaux.be/content/view/801/74/> (Accessed on May 20, 2008).
[29] A. Prowse, The urban decline of the house sparrow, Brit. Birds 95 (2002) 143–146.
[30] A. Balmori, Aves y telefonía móvil. Resultados preliminares de los efectos de las ondas electromagnéticas sobre la fauna urbana, El ecologista 36 (2003) 40–42.
[31] C.K. Chou, A.W. Guy, L.L. Kunz, R.B. Johnson, J.J. Crowley, J.H. Krupp, Long-term, low-level microwave irradiation of rats, Bioelectromagnetics 13 (1992) 469–496.
[32] E.T. Novoselova, E.E. Fesenko, Stimulation of production of tumour necrosis factor by murine macrophages when exposed in vivo and in vitro to weak electromagnetic waves in the centimeter range, Biofizika 43 (1998) 1132–1133.
[33] K.J. Fernie, D.M. Bird, Evidence of oxidative stress in American kestrels exposed to electromagnetic fields, Environ. Res. A 86 (2001) 198–207.
[34] R.C. Beasond, P. Semm, Responses of neurons to an amplitude modulated microwave stimulus, Neurosci. Lett. 33 (2002) 175–178.
[35] K.J. Fernie, D.M. Bird, R.D. Dawson, P.C. Lague, Effects of electromagnetic fields on the reproductive success of American kestrels, Physiol. Biochem. Zool. 73 (2000) 60–65.
[36] K.J. Fernie, N.J. Leonard, D.M. Bird, Behavior of free-ranging and captive American kestrels under electromagnetic fields, J. Toxicol. Environ. Health, Part A 59 (2000) 597–603.
[37] K.J. Fernie, S.J. Reynolds, The effects of electromagnetic fields from power lines on avian reproductive biology and physiology: a review., J. Toxicol. Environ. Health, Part B 8 (2005) 127–140.
[38] K.J. Fernie, D.M. Bird, Effects of electromagnetic fields on body mass and food-intake of American kestrels, Condor 101 (1999) 616–621.
[39] S. Dasdag, M.A. Ketani, Z. Akdag, A.R. Ersay, I. Sar, Ö.C. Demirtas, M.S. Celik, Whole body microwave exposure emitted by cellular phones and testicular function of rats, Urol. Res. 27 (1999) 219–223.
[40] M. Davoudi, C. Brössner, W. Kuber, Der Einfluss elektromagnetischer wellen auf die Spermienmotilität, J. für Urol. Urogynäkol. 9 (2002) 18–22.
[41] I. Fejes, Z. Za Vaczki, J. Szollosi, R.S. Kolosza, J. Daru, L. Kova Cs, L.A. Pa, Is there a relationship between cell phone use and semen quality? Arch. Androl. 51 (2005) 385–393.
[42] P. Stefanis, A. Drakeley, R. Gazvani, D.I. Lewis-Jones, Growing concern over the safety of using mobile phones and male fertility, Arch. Androl. 52 (2006) 9–14.

[43] O. Erogul, E. Oztas, I. Yildirim, T. Kir, E. Aydur, G. Komesli, H.C. Irkilata, M.K. Irmak, A.F. Peker, Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study, Arch. Med. Res. 37 (2006) 840–843.

[44] A. Agarwal, F. Deepinder, R.K. Sharma, G. Ranga, J. Li, Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study, Fertil. Steril. 89 (2008) 124–128.

[45] A. Wdowiak, L. Wdowiak, H. Wiktor, Evaluation of the effect of using mobile phones on male fertility, Ann. Agric. Environ. Med. 14 (1) (2007) 169–172.

[46] J.G. Yan, A.M. Gresti, T. Bruce, Y.H. Yan, A. Granlund, H.S. Matloub, Effects of cellular phone emissions on sperm motility in rats, Fertil. Steril. 88 (4) (2007) 957–964.

[47] P.F. Doherty, T.C. Grubb, Effects of high-voltage power lines on birds breeding within the powerlines' electromagnetic fields, Sialia 18 (1996) 129–134.

[48] V. Garaj-Vrhovac, D. Horvat, Z. Koren, The relationship between colony-forming ability, chromosome aberrations and incidence of micronuclei in V79 Chinese hamster cells exposed to microwave radiation, Mutat. Res. 263 (1991) 143–149.

[49] H. Lai, N.P. Singh, Acute low-intensity microwave exposure increases DNA single-strand breaks in rat brain cells, Bioelectromagnetics 16 (1995) 207–210.

[50] S. Balode, Assessment of radio-frequency electromagnetic radiation by the micronucleus test in bovine peripheral erythrocytes, Sci. Total Environ. 180 (1996) 81–85.

[51] I. Belyaev, L. Hillert, E. Markova, R. Sarimov, L. Malmgren, B. Persson, M. Harms-Ringdahl, Microwaves of mobile phones affect human lymphocytes from normal and hypersensitive subjects dependent on frequency, in: 26th Annual Meeting of the Bioelectromagnetics (BEMS), Washington, USA, 2004.

[52] G. Demsia, D. Vlastos, D.P. Matthopoulos, Effect of 910-MHz electromagnetic field on rat bone marrow, Sci. World J. 4 (2004) 48–54.

[53] Reflex, 2004, <http://www.verum-foundation.de/cgi-bin/content.cgi?id=euprojekte01>.

[54] E. Diem, C. Schwarz, F. Adlkofer, O. Jahn, H. Rudiger, Non-thermal DNA breakage by mobile-phone radiation (1800 MHz) in human fibroblasts and in transformed GFSH-R17 rat granulosa cells in vitro, Mut. Res. 583 (2005) 178–183.

[55] A.G. Gandhi, P. Singh, Cytogenetic damage in mobile phone users: preliminary data, Int. J. Hum. Genet. 5 (2005) 259–265.

[56] A. Di Carlo, N. Wite, F. Guo, P. Garrett, T. Litovitz, Chronic electromagnetic field exposure decreases HSP70 levels and lowers cytoprotection, J. Cell. Biochem. 84 (2002) 447–454.

[57] D. Leszczynski, S. Joenväärä, J. Reivinen, R. Kuokka, Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: molecular mechanism for cancer- and blood-brain barrier-related effects, Differentiation 70 (2002) 120–129.

[58] E. Berman, L. Chacon, D. House, B.A. Koch, W.E. Koch, J. Leal, S. Lovtrup, E. Mantiply, A.H. Martin, G.I. Martucci, K.H. Mild, J.C. Monahan, M. Sandstrom, K. Shamsaifar, R. Tell, M.A. Trillo, A. Ubeda, P. Wagner, Development of chicken embryos in a pulsed magnetic field, Bioelectromagnetics 11 (1990) 169–187.

[59] B.J. Youbicier-Simo, M. Bastide, Pathological effects induced by embryonic and postnatal exposure to EMFs radiation by cellular mobile phones, Radiat. Protect. 1 (1999) 218–223.

[60] A. Úbeda, J. Leal, M.A. Trillo, M.A. Jimenez, J.M.R. Delgado, Pulse shape of magnetic fields influences chick embryogenesis, J. Anat. 137 (1983) 513–536.

[61] J.M. Farrel, T.L. Litovitz, M. Penafiel, The effect of pulsed and sinusoidal magnetic fields on the morphology of developing chick embryos, Bioelectromagnetics 18 (1997) 431–438.

[62] Ju.G. Grigoriew, Influence of the electromagnetic field of the mobile phones on chickens embryo, to the evaluation of the dangerousness after the criterion of this mortality, J. Radiat. Biol. 5 (2003) 541–544.

[63] F. Batellier, I. Couty, D. Picard, J.P. Brillard, Effects of exposing chicken eggs to a cell phone in "call" position over the entire incubation period, Theriogenology 69 (2008) 737–745.

[64] L. Veterány, A. Veterányová, J. Jedlicka, Effect of magnetic field on embryonic mortality, Cesk. Fysiol. 50 (2001) 141–143.

[65] K.B. Hotary, K.R. Robinson, Evidence of a role for endogenous electrical fields in chick embryo development, Development 114 (1992) 985–996.

[66] M. Mevissen, M. Haübler, Acceleration of mammary tumorigenesis by exposure of 7,12-dimethylbenz(a)anthracene-treated female rats in a 50-Hz, 100-μT magnetic field: replication study, J. Toxicol. Environ. Health, Part A 53 (1998) 401–418.

[67] D. Flipo, M. Fournier, C. Benquet, P. Roux, C. Le Boulaire, Increased apoptosis, changes in intracellular Ca^{2+}, and functional alterations in lymphocytes and macrophages after in vitro exposure to static magnetic field, J. Toxicol. Environ. Health, Part A 54 (1998) 63–76.

[68] M. Fedrowitz, K. Kamino, W. Löscher, Significant differences in the effects of magnetic field exposure on 7,12 dimethylbenz (a)anthracene-induced mammary carcinogenesis in two sub-strains of Sprague-Dawley rats, Cancer Res. 64 (2004) 243–251.

[69] A.H. Frey, S.R. Feld, Avoidance by rats of illumination with low power nonionizing electromagnetic energy, J. Comp. Physiol. Psychol. 89 (1975) 183–188.

[70] M.A. Navakatikian, L.A. Tomashevskaya, Phasic behavioral and endocrine effects of microwaves of nonthermal intensity, in: D.O. Carpenter (Ed.), Biological Effects of Electric and Magnetic Fields, 1, Academic Press, San Diego, CA, 1994.

[71] D.D. Krstić, B.J. Đinđić, D.T. Sokolović, V.V. Marković, D.M. Petković, S.B. Radić, The results of experimental exposition of mice by mobile telephones, in: TELSIKS Conference, Serbia and Montenegro, Microw. Rev. (2005) 34–37.

[72] I.U.G. Grigoriev, S.N. Luk'ianova, V.P. Makarov, V.V. Rynskov, N.V. Moiseeva, Motor activity off rabbits in conditions of chronic low-intensity pulse microwave irradiation, Radiat. Biol. Radioecol. 35 (1995) 29–35.

[73] B. Nicholls, P.A. Racey, Bats avoid radar installations: Could electromagnetic fields deter bats from colliding with wind turbines? PLOS One 3 (2007) e297.

[74] A. Balmori Murciélago rabudo–*Tadarida teniotis*, En: Enciclopedia Virtual de los Vertebrados Españoles, Carrascal, L.M., Salvador, A. (Eds.), Museo Nacional de Ciencias Naturales, Madrid, 2004c, <http://www.vertebradosibericos.org/>.

[75] T.A. Marks, C.C. Ratke, W.O. English, Strain voltage and developmental, reproductive and other toxicology problems in dogs, cats and cows: a discussion, Vet. Human Toxicol. 37 (1995) 163–172.

[76] W. Löscher, G. Käs, Conspicuous behavioural abnormalities in a dairy cow herd near a TV and radio transmitting antenna, Pract. Vet. Surg. 29 (1998) 437–444.

[77] A. Yurekli, M. Ozkan, T. Kalkan, H. Saybasili, H. Tuncel, P. Atukeren, K. Gumustas, S. Seker, GSM Base Station Electromagnetic Radiation and Oxidative Stress in Rats, Electromagn. Biol. Med. 25 (2006) 177–188.

[78] S. Tofani, G. Agnesod, P. Ossola, S. Ferrini, R. Bussi, Effects of continuous low-level exposure to radio-frequency radiation on intrauterine development in rats, Health Phys. 51 (1986) 489–499.

[79] T.P. Moorhouse, D.W. Macdonald, Indirect negative impacts of radio-collaring: sex ratio variation in water voles, J. Appl. Ecol. 42 (2005) 91.

[80] R.F. McGivern, R.Z. Sokol, W.R. Adey, Prenatal exposure to a low-frequency electromagnetic field demasculinizes adult scent marking behavior and increases accessory sex organ weights in rats, Teratology 41 (1990) 1–8.

[81] G.M. Lee, R.R. Neutra, L. Hristova, M. Yost, R.A. Hiatt, A Nested Case-Control Study of Residential and Personal Magnetic Field Measures and Miscarriages, Epidemiology 13 (2002) 21–31.

[82] A.Y. Rezk, K. Abdulqawi, R.M. Mustafa, T.M. Abo El-Azm, H. Al-Inany, Fetal and neonatal responses following maternal exposure to mobile phones, Saudi Med. J. 29 (2008) 218–223.

[83] L.G. Salford, A.E. Brun, J.L. Eberhardt, L. Malmgren, B.R. Persson, Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones, Environ. Health Perspect. 111 (2003) 881–893.

[84] D. Adang, B. Campo, A.V. Vorst, Has a 970 MHz Pulsed exposure an effect on the memory related behaviour of rats? in: The 9th European Conference onWireless Technology, September 2006, 2006, pp.

[85] A.A. Kolodynski, V.V. Kolodynska, Motor and psychological functions of school children living in the area of the Skrunda Radio Location Station in Latvia, Sci. Total Environ. 180 (1996) 87–93.

[86] H.A. Divan, L. Kheifets, C. Obel, J. Olsen, Prenatal and postnatal exposure to cell phone use and behavioral problems in children, Epidemiology 19 (2008) 523–529.

[87] K. Mann, J. Roschkle, Effects of pulsed high-frequency electromagnetic fields on human sleep, Neuropsychobiology 33 (1996) 41–47.

[88] A.V. Kramarenko, U. Tan, Effects of high-frequency electromagnetic fields on human EEG: a brain mapping study, Int. J. Neurosci. 113 (2003) 1007–1019.

[89] A.A. Marino, E. Nilsen, C. Frilot, Nonlinear changes in brain electrical activity due to cell phone radiation, Bioelectromagnetics 24 (2003) 339–346.

[90] A.R. Blaustein, P.T.J. Johnson, Explaining frog deformities, Sci. Am. 288 (2003) 60–65.

[91] A. Balmori, The incidence of electromagnetic pollution on the amphibian decline: is this an important piece of the puzzle? Toxicol. Environ. Chem. 88 (2006) 287–299.

[92] W.C. Levengood, A new teratogenic agent applied to amphibian embryos, J. Embryol. Exp. Morphol. 21 (1969) 23–31.

[93] R.H. Landesman, W. Scott Douglas, Abnormal limb regeneration in adult newts exposed to a pulsed electromagnetic field, Teratology 42 (1990) 137–145.

[94] N.M. Grefner, T.L. Yakovleva, I.K. Boreysha, Effects of electromagnetic radiation on tadpole development in the common frog (*Rana temporaria* L.), Russ. J. Ecol. 29 (1998) 133–134.

[95] A. Balmori, in preparation: Phone masts effects on common frog (*Rana temporaria*) tadpoles: An experiment in the city. See the video clips in: http://www.hese-project.org/hese-uk/en/issues/nature.php?id=frogs.

[96] U. Warnke, Bienen, vögel und menschen, Die Zerstörung der Natur durch "Elektrosmog". Kompetenzinitiative, 2007 46 pp.

[97] R.L. Carpenter, E.M. Livstone, Evidence for nonthermal effects of microwave radiation: Abnormal development of irradiated insect pupae, IEEE Trans. Microw. Theor. Tech. 19 (1971) 173–178.

[98] D. Weisbrot, H. Lin, L. Ye, M. Blank, R. Goodman, Effects of mobile phone radiation on reproduction and development in *Drosophila melanogaster*, J. Cell. Biochem. 89 (2003) 48–55.

[99] D.J. Panagopoulos, A. Karabarbounis, L.H. Margaritis, Effect of GSM 900 MHz Mobile Phone Radiation on the Reproductive Capacity of *Drosophila melanogaster*, Electromagn. Biol. Med. 23 (2004) 29–43.

[100] D.J. Panagopoulos, E.D. Chavdoula, A. Karabarbounis, L.H. Margaritis, Comparison of bioactivity between GSM 900 MHz and DCS 1800 MHz mobile telephony radiation, Electromagn. Biol. Med. 26 (2007) 33–44.

[101] A. Balmori, Efectos de las radiaciones electromagnéticas de la telefonía móvil sobre los insectos, Ecosistemas (2006).

[102] H. Stever, J. Kuhn, C.Otten, B.Wunder, W. Harst, Verhaltensanderung unter elektromagnetischer Exposition. Pilotstudie, Institut für mathematik. Arbeitsgruppe, Bildungsinformatik. Universität Koblenz-Landau, 2005.

[103] V.G. Balodis, K. Brumelis, O. Kalviskis, D. Nikodemus, V.Z. y Tjarve, Does the Skrunda radio location station diminish the radial growth of pine trees? Sci. Total Environ. 180 (1996) 57–64.

[104] T. Selga, M. Selga, Response of *Pinus Sylvestris* L. needles to electromagnetic fields. Cytological and ultraestructural aspects, Sci. Total Environ. 180 (1996) 65–73.

[105] I. Magone, The effect of electromagnetic radiation from the Skrunda Radio Location Station on Spirodela polyrhiza (L.) Schleiden cultures, Sci. Total Environ. 180 (1996) 75–80.

[106] D.D. Sandu, C. Goiceanu, A. Ispas, I. Creanga, S. Miclaus, D.E. Creanga, A preliminary study on ultra high frequency electromagnetic fields effect on black locust chlorophylls, Acta Biol. Hung. 56 (2005) 109–117.

[107] D. Roux, Al. Vian, S. Girard, P. Bonnet, F. Paladian, E. Davies, G. Ledoigt, High frequency (900 MHz) low amplitude (5 V m^{-1}) electromagnetic field: a genuine environmental stimulus that affects transcription, translation, calcium and energy charge in tomato, Planta 227 (2007) 883–891.

[108] M. Tkalec, K. Malarik, B. Pevalek-Kozlina, Exposure to radiofrequency radiation induces oxidative stress in duckweed *Lemna minor* L., Sci. Total Environ. 388 (2007) 78–89.

[109] A. Balmori, ¿Pueden afectar las microondas pulsadas emitidas por las antenas de telefonía a los árboles y otros vegetales? Ecosistemas (2004), http://www.revistaecosistemas.net/articulo.asp?Id=29&Id_Categoria=1&tipo=otros_contenidos.

[110] V. Schorpp, 2007, <http://www.puls-schlag.org/baumschaeden.htm#linden>.

[111] A. Balmori, Posibles efectos de las ondas electromagnéticas utilizadas en la telefonía inalámbrica sobre los seres vivos, Ardeola 51 (2004) 477–490.

ELSEVIER

Pathophysiology 16 (2009) 201–204

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

FM-radio and TV tower signals can cause spontaneous hand movements near moving RF reflector

Paavo Huttunen[a,*], Osmo Hänninen[b], Risto Myllylä[a]

[a] *Laboratory of Optoelectronics and Measurement Technology, University of Oulu, P.O. Box 4500, 90014 Oulu, Finland*
[b] *Department of Physiology, University of Kuopio, P.O. Box 1627, 70211 Kuopio, Finland*

Received 2 January 2009; received in revised form 23 January 2009; accepted 30 January 2009

Abstract

For testing human sensitivity to radio frequency (RF) standing waves a movable reflecting wall was constructed. Radio waves from the radio–TV tower reflected back and formed a standing wave near the reflector. When the reflector was moved, the position of the maximums of the standing waves changed and the electromagnetic intensity changed in the body of the standing test subject. The computer with an AD-converter registered the signals of the hand movement transducer and the RF-meter with 100 MHz dipole antennas. A total of 29 adults of different ages were tested. There were 9 persons whose hand movement graphs included features like the RF-meter. Six showed responses that did not correlate with the RF-meter. There were also 14 persons who did not react at all. Sensitive persons seem to react to crossing standing waves of the FM-radio or TV broadcasting signals.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Sensorimotor responses; Radio frequency standing waves

1. Introduction

Radio frequency radiation (RFR) has been studied intensively in the near GHz region. Subjective symptoms, sleeping problems and cognitive performance have been reported in subjects living near mobile phone base stations [1]. In the recent past, frequencies of FM-radio and television (TV) signals have been much less studied even though these frequencies cause biological and health effects, too. The whole body resonance frequency of an average man and thus the maximum absorption of RF energy occur at 70–80 MHz [2]. This is near the frequencies used in very high frequency (VHF) broadcasting. The head and limbs absorb much more energy than the torso at frequencies above body resonance [3]. Greatest absorption in the head region of man occurs at a frequency of about 375 MHz [4]. Absorption is stronger for wave propagation from head to toe than it is when the electric field is parallel to the long axis. The authors [4] believed that the enchanced absorption in the head region may make head resonance significant in the study of behavioral effects, blood–brain barrier permeability, cataractogenesis, and other microwave bioeffects. Even increased health risks like cancer, especially melanoma incidence, near FM broadcasting and television transmitters have been reported [5,6].

Nerve impulses initiate muscle contraction by calcium ion release from the sarcoplasmic reticulum, which takes place when electric nerve signals reach the plasma membrane and T-tubules of muscle fibers [7]. Voltage dependent Ca-channels open. Acetylcholine esterase (AChE) breaks down the acetylcholine, and Na-channels close [7]. It has been reported that the number of Ca^{2+} ions liberated from hen's frontal brain depends on the modulation frequency of the weak VHF radiation, with a maximum at a frequency of 16 Hz, while an unmodulated field causes no ion release [2,8]. Multiple RF power-density windows in calcium ion release from brain tissue have presented [9]. A significant decrease in AChE activity has been found in rats exposed to radio frequency radiation of 147 MHz and its sub-harmonics 73.5 and 36.75 MHz amplitude modulated at 16 and 76 Hz. A decrease in AChE activity was independent of carrier wave frequencies [10].

* Corresponding author.
E-mail address: paavo.huttunen@elisanet.fi (P. Huttunen).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.002

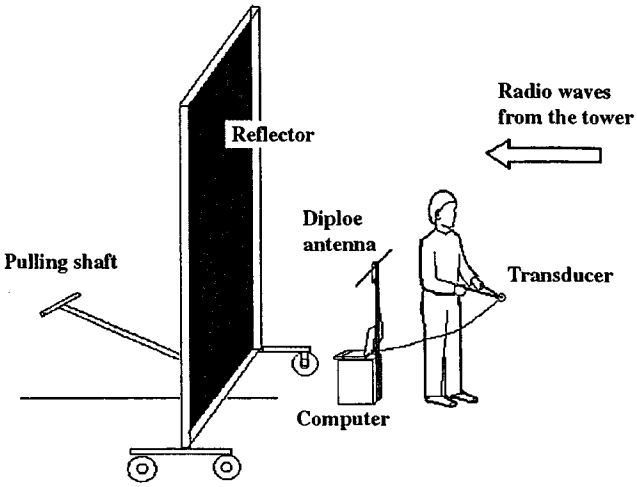


Fig. 1. Testing human radio wave sensitivity. Radio waves from the TV tower reflect back from the reflector and form a standing wave. When the reflector moves, the position of the maximums of the standing wave change, and the electromagnetic intensity changes in the body of the test subject. The computer with an AD-converter registers the signals of hand movement transducer and the RF-meter with the dipole antennas.

As there is previous evidence from human and animal studies that electromagnetic irradiation has effects in the brain, the aim of the present study was to find out, if the motor responses are generated in sensitive persons, when they move across a set of standing waves caused by radiation of a FM-radio and TV tower. The connection between the hand movements and the integrated intensity of electromagnetic field of FM-radio broadcasting were recorded.

2. Methods

The wavelength of a 100-MHz radio wave is 3 m. For testing human sensitivity to moving standing waves a movable reflecting wall with wooden frame 3 m height and 5 m wide was constructed (Fig. 1). Steel net of 20 mm × 20 mm mesh was used. Five horizontal net slices of 60 cm wide were bound together with steel wire forming a radio waves reflecting surface. The test place was 5 km from the FM-radio tower. The frame was placed in an open field perpendicular to the incoming wave. The test subject was standing back towards the frame, and he had the hand movement transducer in his hands. The RF-meter with horizontal dipole antenna was close behind him. When started, the frame was 2 m from his back and it was moved 20 m forth and back. The computer registered both signals. The method and the aim of the test were at first presented, in brief, to the test persons. All together 29 adult persons of different ages were tested. They were participants in a seminar relating to effects of electric fields, and thus they possibly do not represent a normal population.

The broadband (30–300 MHz) RF-meter and the hand movement transducer were constructed for this study by the authors. The signals were digitised by Pico high resolution

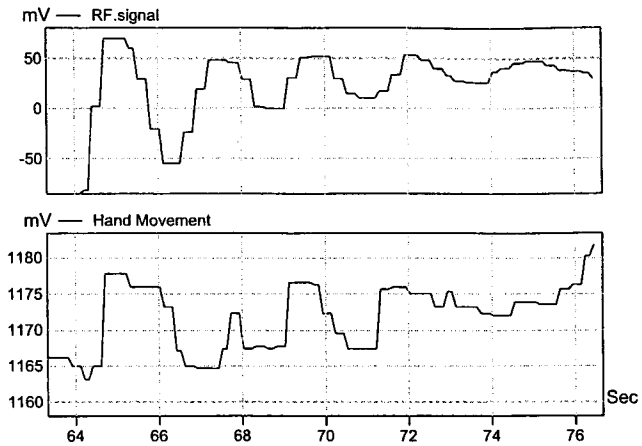


Fig. 2. Hand movements near the moving RF reflector. The standing waves moved slowly with the reflector. Intensity of the electric field was measured with the broadband RF-meter with horizontal dipole antennas. Variation of the field intensity is presented in the upper curve and the hand movements of the standing test person are in the lower curve.

data logger (ADC16). The radio frequency spectrum was measured using a spectrum analyser (GW instek GSP-827, 2.7 GHz) with 1.5 m horizontal dipole antennas. When measured, the antenna was fastened to a wooden frame 1 m from the ground.

3. Results and discussion

Results on the movable frame showed different hand movement reactions of the test subjects. There were 9 persons who reacted like the RF-meter (Fig. 2), 6 persons whose graphs, though obvious, showed no correlation to the RF-meter and 14 persons who did not react or showed only small noise like changes in their graphs (Table 1). Spectrum at the test place contains mainly the FM-radio broadcasting signals and four digital TV signals (Fig. 3). Most prominent (85 dB μV, approximately 50 mV/m) are the 6 horizontally polarized FM-radio signals (Fig. 4).

Resonances in body parts affects the power absorption. Theoretically, the optimal length of a thin antenna in radio-frequency reception is nearly half of the wavelength of the

Table 1
Reactions to standing waves of FM-radio signals. Classification of results of 29 tested persons. Test subject was standing and the radio wave reflector was moved behind him/her. The hand movement graphs were compared to the graphs of the broadband radio frequency (RF) meter.

Reactions to standing waves	9 persons	Hand movement graphs include features like graphs of RF-meter.
Possible reaction	6 persons	Changes in the graphs but no correlation to RF-meter.
No reaction	14 persons	Only small noise like changes in the graphs.

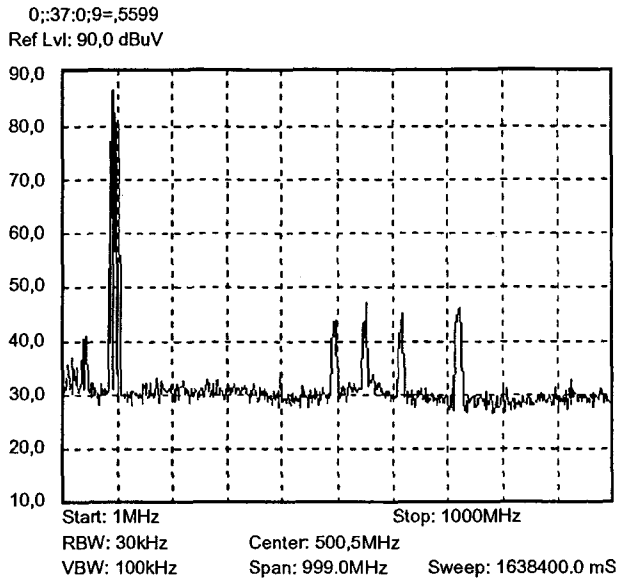


Fig. 3. Spectrum 1–1000 MHz at the test place. The highest peaks at the left are FM-radio broadcasting signals and the four lower peaks in the middle are the digital TV signals. Because the measurement was made with 1.5 m dipoles, signals near 100 MHz are more prominent because of antenna resonance.

incoming radio wave. The experimental maximum whole body resonance frequency is lower than the resonance frequency for an ideal half wave dipole antenna [11]. The whole body resonance length of a human at the frequencies of 80–108 MHz applied to FM broadcasting is about 1.1–1.5 m. Because in this experiment the test subjects were standing and the 100 MHz FM-radio signals and TV signals at higher frequencies are horizontally polarized, the absorption is obviously higher in the shoulder area. The distance between two maximums of the 100 MHz standing wave is 1.5 m. The half

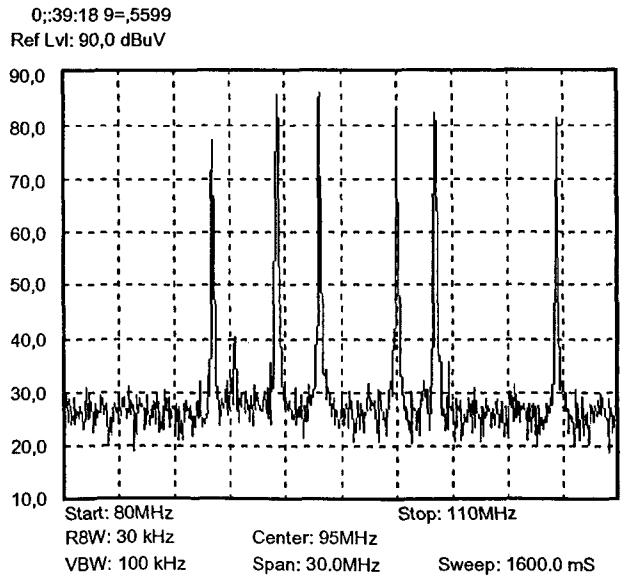


Fig. 4. Spectrum of the FM-radio broadcasting at the test place. Six channels were sending and the maximum electric field intensity was 85 dB μV.

waves of local digital TV signals (500–700 MHz) are only about 20–30 cm. This means that there can be many maximums of standing waves of TV signals in the body at the same time, even near the reflector.

The biggest variation in the local field intensity was caused by the FM broadcasting. There were 6 channels in the tower. Because of different wave lengths, the standing waves near the reflector are at the same phase and they amplify each other, but further away, the phases are mixed and so the amplitude of the summed standing waves is smaller.

With this experiment, we cannot exactly say where the reaction occurs, in limbs, muscles or in the head. It is possible that a change of intensity in standing radiowaves causes a small change in the nerve-muscle permeability of the nerve signal. The person feels it like a spontaneous muscle contraction. His hands are moving away and closer when the standing waves are passing. By some persons, the distance from hand to hand varied 0–60 cm. That means that some of muscles in arms and shoulders should react.

The spectrum contains many frequencies of electromagnetic radiation. The radiation is not only coming from the nearest tower, and it is impossible to clean the test area from other waves. This experiment was made at rural area, but even there, the private hand held telephone signals cause interferences to RF-instruments.

4. Conclusions

Sensitive persons seem to react to crossing standing waves of the FM-radio or TV broadcasting signals. The reactions were apparently initiated by RFR near reflecting objects, but they became more random in very weak variations of total field intensity. In any case, individuals are different, and in natural situations many sources interfere with each other.

References

[1] H.-P. Hutter, H. Moshammer, P. Wallner, M. Kundi, Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations, Occup. Environ. Med. 63 (2006) 307–313.

[2] R.V. Adey, Frequency and power windowing in tissue interactions with weak electromagnetic fields, Proc. IEEE 68 (1) (1980) 119–125.

[3] R.G. Olsen, T.A. Griner, Specific absorption rate in mondels of man and monkey at 225 and 2,000 MHz, Bioelectromagnetics 8 (1987) 377–384.

[4] M.J. Hagmann, O.P. Gandhi, J.A. D'andrea, I. Chatterjee, Head resonance: numerical solutions and experimental results, IEEE Trans. Microw. Theory Tech. MTT-27 (9) (1979) 809–813.

[5] H.G. Dolk, P. Shaddik, Walls, et al., Cancer incidence near radio and television transmitters in Great Britain I and II, Am.J. Epidemiol. 145 (1997) 1–17.

[6] Ö. Hallberg, O. Johansson, Melanoma incidence and frequency modulation (FM) broadcasting., Arch. Environ. Health 57 (1) (2002) 32–40.

[7] B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts, J.D. Watson (Eds.), Moleclar Biology of the Cell, The Nervous System, Garland Publishing Inc., New York/London, 1983, pp. 1013–1098 (Chapter 18).

[8] C.F. Blackman, J.A. Elder, C.M. Weil, S.G. Benane, D.C. Eichinger, D.E. House, Induction of calcium-ion efflux from brain tissue by radiofrequency radiation: effects of modulation frequency and field strength, Radio Sci. 14 (1979) 93–98.

[9] C. Blackman, L.S. Kinney, D.E. House, W.T. Joines, Multiple power-density windows and their possible origin, Bioelectromagnetics 10 (2) (1989) 115–128.

[10] K.K. Kunjilwar, J. Behari, Effects of amplitude-modulated radio frequency radiation on cholinergic system of developing rats, Brain Res. 601 (1–2) (1993) 321–324.

[11] O.P. Gandhi, State of the knowledge for electromagnetic absorbed dose in man and animals (1980), Proc. IEEE 68 (1980) 24–32.

ELSEVIER

Pathophysiology 16 (2009) 205–216

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Cell phone radiation: Evidence from ELF and RF studies supporting more inclusive risk identification and assessment☆

Carl Blackman

Raleigh, NC 27607, USA

Received 21 January 2009; received in revised form 3 February 2009; accepted 3 February 2009

Abstract

Many national and international exposure standards for maximum radiation exposure from the use of cell phone and other similar portable devices are ultimately based on the production of heat particularly in regions of the head, that is, thermal effects (TE). The recent elevation in some countries of the allowable exposure, that is, averaging the exposure that occurs in a 6 min period over 10 g of tissue rather than over 1 g allows for greater heating in small portions of the 10-g volume compared to the exposure that would be allowed averaged over 1-g volume. There is concern that 'hot' spots, that is, momentary higher intensities, could occur in portions of the 10-g tissue piece, might have adverse consequences, particularly in brain tissue.

There is another concern about exposure to cell phone radiation that has been virtually ignored except for the National Council of Radiation Protection and Measurements (NCRP) advice given in a publication in 1986 [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.]. This NCRP review and guidance explicitly acknowledge the existence of non-thermal effects (NTE), and included provisions for reduced maximum-allowable limits should certain radiation characteristics occur during the exposure.

If we are to take most current national and international exposure standards as completely protective of thermal injury for acute exposure only (6 min time period) then the recent evidence from epidemiological studies associating increases in brain and head cancers with increased cell phone use per day and per year over 8–12 years, raises concerns about the possible health consequences on NTE first acknowledged in the NCRP 1986 report [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.].

This paper will review some of the salient evidence that demonstrates the existence of NTE and the exposure complexities that must be considered and understood to provide appropriate, more thorough evaluation and guidance for future studies and for assessment of potential health consequences. Unfortunately, this paper is necessary because most national and international reviews of the research area since the 1986 report [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.] have not included scientists with expertise in NTE, or given appropriate attention to their requests to include NTE in the establishment of public-health-based radiation exposure standards. Thus, those standards are limited because they are not comprehensive.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Non-thermal effects; Electromagnetic fields; Exposure standards

1. Introduction

1.1. The current approach to exposure limits (based on heating and electric current flow in tissues)

It is universally accepted that radiofrequency radiation (RFR) can cause tissue heating (thermal effects, TE) and that extremely low-frequency (ELF) fields, e.g., 50

☆ Disclaimer: The opinions expressed in this text are those of its author, and are not necessarily those of his employer, the U.S. Environmental Protection Agency.

E-mail address: Carl.Blackman@gmail.com.

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.02.001

and 60 Hz, can cause electrical current flows that shock and even damage or destroy tissues. These factors alone are the underlying bases for present exposure standards. EMF exposures that cause biological effects at intensities that do not cause obvious thermal changes, that is, non-thermal effects (NTE), have been widely reported in the scientific literature since the 1970s including beneficial applications in development and repair processes. The current public safety limits do not take modulation into account and thus are no longer sufficiently protective of public health where chronic exposure to pulsed or pulse-modulated signal is involved, and where sub-populations of more susceptible individuals may be at risk from such exposures.

1.2. Modulation as a critical element

Modulation signals are one important component in the delivery of EMF signals to which cells, tissues, organs and individuals can respond biologically. At the most basic level, modulation can be considered a pattern of pulses or repeating signals which have specific meaning in defining that signal apart from all others. Modulated signals have a specific 'beat' defined by how the signal varies periodically or aperiodically over time. Pulsed signals occur in an on–off pattern, which can be either smooth and rhythmic, or sharply pulsed in quick bursts. Amplitude and frequency modulation involves two very different processes where the high-frequency signal, called the carrier wave, has a lower frequency signal that is superimposed on or 'rides' on the carrier frequency. In amplitude modulation, the lower frequency signal is embedded on the carrier wave as changes in its amplitude as a function of time, whereas in frequency modulation, the lower frequency signal is embedded as slight changes in the frequency of the carrier wave. Each type of low-frequency modulation conveys specific 'information', and some modulation patterns are more effective (more bioactive) than others depending on the biological reactivity of the exposed material. This enhanced interaction can be a good thing for therapeutic purposes in medicine, but can be deleterious to health where such signals could stimulate disease-related processes, such as increased cell proliferation in precancerous lesions. Modulation signals may interfere with normal, non-linear biological functions. More recent studies of modulated RF signals report changes in human cognition, reaction time, brainwave activity, sleep disruption and immune function. These studies have tested the RF and ELF-modulated RF signals from emerging wireless technologies (cell phones) that rely on pulse-modulated RF to transmit signals. Thus modulation can be considered as information content embedded in the higher frequency carrier wave that may have biological consequences beyond any effect from the carrier wave directly.

In mobile telephony, for example, modulation is one of the underlying ways to categorize the radiofrequency signal of one telecom carrier from another (TDMA from CDMA from GSM). Modulation is likely a key factor in determining whether and when biological reactivity might be occurring, for example in the new technologies which make use of modulated signals, some modulation (the packaging for delivery for an EMF 'message') may be bioactive, for example, when frequencies are similar to those found in brain wave patterns. If a new technology happens to use brain wave frequencies, the chances are higher that it will have effects, in comparison, for example, to choosing some lower or higher modulation frequency to carry the same EMF information to its target.

This chapter will show that other EMF factors may also be involved in determining if a given low-frequency signal directly, or as a modulation of a radiofrequency wave, can be bioactive. Such is the evolving nature of information about modulation. It argues for great care in defining standards that are intended to be protective of public health and well-being. This chapter will also describe some features of exposure and physiological conditions that are required in general for non-thermal effects to be produced, and specifically *to illustrate how modulation is a fundamental factor which should be taken into account in public safety standards.*

2. Laboratory evidence

Published laboratory studies have provided evidence for more than 40 years on bioeffects at much lower intensities than cited in the various widely publicized guidelines for limits to prevent harmful effects. Many of these reports show EMF-caused changes in processes associated with cell growth control, differentiation and proliferation, that are biological processes of considerable interest to physicians for potential therapeutic applications and for scientists who study the molecular and cellular basis of cancer. EMF effects have been reported in gene induction, transmembrane signaling cascades, gap junction communication, immune system action, rates of cell transformation, breast cancer cell growth, regeneration of damaged nerves and recalcitrant bone-fracture healing. These reports have cell growth control as a common theme. Other more recent studies on brainwave activity, cognition and human reaction time lend credence to modulation (pulsed RF and ELF-modulated RF) as a concern for wireless technologies, most prominently from cell phone use.

In the process of studying non-thermal biological effects, various exposure parameters have been shown to influence whether or not a specific EMF can cause a biological effect, including intensity, frequency, the co-incidence of the static magnetic field (both the natural earth's magnetic field and anthropogenic fields), the presence of the electrical field, the magnetic field, or their combination, and whether EMF is sinusoidal, pulsed or in more com-

plex wave forms. These parameters will be discussed below.

Experimental results will be used to illustrate the influence of each EMF parameter, while also demonstrating that it is highly unlikely the effects are due to EMF-caused current flow or heating.

2.1. Initial studies that drew attention to NTE

Several papers in the 1960s and early 1970s reported that ELF fields could alter circadian rhythms in laboratory animals and humans. In the latter 1960s, a paper by Hamer [2] reported that the EMF environment in planned space capsules could cause human response time changes, i.e., the interval between a signal and the human response. Subsequent experiments by a research group led by Adey were conducted with monkeys, and showed similar response time changes and also EEG pattern changes [3,4]. The investigators shifted the research subject to cats and decided they needed to use a radiofrequency field to carry the ELF signal into the cat brain, and observed EEG pattern changes, ability to sense and behaviorally respond to the ELF component of RFR, and the ability of minor electric current to stimulate the release of an inhibitory neurotransmitter, GABA, and simultaneous release of a surrogate measure, calcium ions, from the cortex [5,6]. At this time Bawin, a member of the research group, adopted newly hatch chickens as sources of brain tissue and observed changes in the release of calcium ions from in vitro specimens as a function of ELF frequency directly or as amplitude modulation ('am') of RFR (RFRam) [7–11]. Tests of both EMF frequency and intensity dependences demonstrated a single sensitive region (termed 'window') over the range of frequency and intensity examined. This series of papers showed that EMF-induced changes could occur in several species (human, monkey, cat and chicken), that calcium ions could be used as surrogate measures for a neurotransmitter, that ELF fields could produce effects similar to RFRam (note: without the 'am', there was no effect although the RFR intensity was the same), and that the dose and frequency response consisted of a single sensitivity window.

Subsequent, independent research groups published a series of papers replicating and extending this earlier work. Initial studies by Blackman, Joines and colleagues [12–25] used the same chick brain assay system as Bawin and colleagues. These papers reported multiple windows in intensity and in frequency within which calcium changes were observed in the chick brain experimental systems under EMF exposure. Three other independent groups offered confirmation of these results by reporting intensity and frequency windows for calcium, neurotransmitter or enolase release under EMF exposure of human and animal nervous system-derived cells in vitro by Dutta et al. [26–29], of rat pancreatic tissue slices by Albert et al. [30], and of frog heart by Schwartz et al. [31] but not frog-heart atrial strips in vitro [32]. This series of papers showed that multiple frequency and intensity windows were a common phenomenon that required the development of new theoretical concepts to provide a mechanism of action paradigm.

2.2. Refined laboratory studies reveal more details

Additional aspects of the EMF experiments with the chick brain described by Blackman and colleagues, above, also revealed critical co-factors that influenced the action of EMF to cause changes in calcium release, including the influence of the local static magnetic field, and the influence of physico-chemical parameters, such as pH, temperature and the ionic strength of the bathing solution surrounding the brain tissue during exposure. This information provides clues for and constraints on any theoretical mechanism that is to be developed to explain the phenomenon. Most current theories ignore these parameters that need to be monitored and controlled for EMF exposure to produce NTE. These factors demonstrate that the current risk assessment paradigms, which ignore them, are incomplete and thus may not provide the level of protection currently assumed.

2.3. Sensitivity of developing organisms

An additional study was also conducted to determine if EMF exposure of chicken eggs while the embryo was developing could influence the response of brain tissue from the newly hatched chickens. The detailed set of frequency and intensity combinations under which effects were observed, were all obtained from hatched chickens whose eggs were incubated for 21 days in an electrically heated chamber containing 60-Hz fields. Thus tests were performed to determine if the 60-Hz frequency of ELF fields (10 V/m in air) during incubation, i.e., during embryogenesis and organogenesis, would alter the subsequent calcium release responses of the brain tissue to EMF exposure. The reports of Blackman et al. [19] and Joines et al. [25] showed that the brain tissue response was changed when the field during the incubation period was 50 Hz rather than 60 Hz. This result is consistent with an anecdotal report of adult humans, institutionalized because of chemical sensitivities, who were also responsive to the frequency of power-line EM fields that were present in the countries where they were born and raised [33]. This information indicates there may be animal and human exposure situations where EMF imprinting during development could be an important factor in laboratory and epidemiological situations. EMF imprinting, which may only become manifest when a human is subjected to chemical or biological stresses, could reduce ability to fight disease and toxic insult from environmental pollution, resulting in a population in need of more medical services, with resulting lost days at work.

3. Fundamental exposure parameters—to be considered when establishing a mode (or mechanism) of action for non-thermal EMF-induced biological effects

3.1. Intensity

There are numerous reports of biological effects that show intensity "windows", that is, regions of intensity that cause changes surrounded by higher and lower intensities that show no effects from exposure. One very clear effect by Blackman and colleagues is 16-Hz, sine wave-induced changes in calcium efflux from brain tissue in a test tube because it shows two very distinct and clearly separated intensity windows of effects surrounded by regions of intensities that caused no effects [17]. There are other reports for similar multiple windows of intensity in the radiofrequency range [22,26,29,31]. Note that calcium ions are a secondary signal transduction agent active in many cellular pathways. These results show that intensity windows exist, they display an unusual and unanticipated "non-linear" (non-linear and non-monotonic) phenomenon that has been ignored in all risk assessment and standard setting exercises, save the NCRP 1986 publication [1]. Protection from multiple intensity windows has never been incorporated into any risk assessment; to do so would call for a major change in thinking. These results mean that lower intensity is not necessarily less bioactive, or less harmful.

Multiple intensity windows appeared as an unexpected phenomenon in the late 1970s and 1980s. There has been one limited attempt to specifically model this phenomenon by Thompson et al. [34], which was reasonably successful. This modeling effort should be extended because there are publications from two independent research groups showing multiple intensity windows for 50, 147, and 450 MHz fields when amplitude modulated at 16 Hz using the calcium ion release endpoint in chicken brains, in vitro. The incident intensities (measured in air) for the windows at the different carrier frequencies do not align at the same values. However, Joines et al. [23,24] and Blackman et al. [20] noted the windows of intensity align across different carrier frequencies if one converts the incident intensity to the intensity expected within the sample at the brain surface. This conversion was accomplished by correcting for the different dielectric constants of the sample materials due to the different carrier frequencies. The uniqueness of this response provides a substantial clue to theoreticians but it is interesting and disappointing that no publications have appeared attempting to address this relationship. It is obvious that this phenomenon is one that needs further study.

3.2. Frequency

Frequency-dependent phenomena are common occurrences in nature. For example, the human ear only hears a portion of the sound that is in the environment, typically from 20 to 20,000 Hz, which is a frequency "window". Another biological frequency window can be observed for plants grown indoors. Given normal indoor lighting the plants may grow to produce lush vegetation but not produce flowers unless illuminated with a lamp that emits a different spectrum of light partially mimicking the light from the sun. Thus, frequency windows of response to various agents exist in biological systems from plants to homo sapiens.

In a similar manner, there are examples of EMF-caused biological effects that occur in a frequency-dependent manner that cannot be explained by current flow or heating. The examples include reports of calcium ion efflux from brain tissue in vitro by Blackman and Joines and colleagues at low frequency [15,19] and at high frequency modulated at low frequency [20,35,24]. An additional example of an unexpected result is by Liboff [36].

In addition, two apparently contradictory multiple-frequency exposure results provide examples of the unique and varied non-thermal interactions of EMF with biological systems. Litovitz and colleagues showed that an ELF sinusoidal signal could induce a biological response in a cell culture preparation, and that the addition of a noise signal of equal average intensity could block the effect caused by the sinusoidal signal, thereby negating the influence of the sinusoidal signal [37]. Similar noise canceling effects were observed using chick embryo preparations [38,39]. It was also shown that the biological effects caused by microwave exposures imitating cell phone signals could be mitigated by ELF noise [40]. However, this observation should not be generalized; a noise signal is not always benign. Milham and Morgan [41] showed that a sinusoidal ELF (60-Hz) signal was not associated with the induction of cancer in humans, but when that sinusoidal signal was augmented by a noise signal, basically transients that added higher frequencies, an increase in cancer was noted in humans exposed over the long-term. Thus, the addition of noise in this case was associated with the appearance of a health issue. Havas [42–44] has described other potential health problems associated with these higher frequency transients, termed "dirty power." The bioactive frequency regions observed in these studies have never been explicitly considered for use in any EMF risk assessments, thus demonstrating the incomplete nature of current exposure guideline limits.

There are also EMF frequency-dependent alterations in the action of nerve growth factor (NGF) to stimulate neurite outgrowth (growth of primitive axons or dendrites) from a peripheral-nerve-derived cell (PC-12) in culture shown by Blackman et al. [45,46] and by Trillo et al. [47]. The combined effect of frequency and intensity is also a common occurrence in both the analogous sound and the light examples given above. Too much or too little of either frequency or intensity show either no or undesirable effects. Similarly, Blackman et al. [15] has reported EMF responses composed of effect "islands" of intensity and frequency combinations, surrounded by a "sea" of intensity and frequency combinations of null effects. Although the mechanisms responsible

for these effects have not been established, the effects represent a here-to-fore unknown phenomenon that may have complex ramifications for risk assessment and standard setting. Nerve growth and neurotransmitter release that can be altered by different combinations of EMF frequencies and intensities, especially in developing organisms like children, could conceivably produce over time a subsequent altered ability to successfully or fully respond behaviorally to natural stressors in the adult environment; research is urgently needed to test this possibility in animal systems.

Nevertheless, this phenomenon of frequency dependence is ignored in the development of present exposure standards. These standards rely primarily on biological responses to intensities within an arbitrarily defined engineering-based frequency bands, not biologically based response bands, and are solely based on an energy deposition determinations.

4. Static magnetic field—a completely unexpected complexity

The magnetic field of the earth at any given location has a relatively constant intensity as a function of time. However, the intensity value, and the inclination of the field with respect to the gravity vector, varies considerable over the face of the earth. More locally, these features of the earth's magnetic field can also vary by more than 20% inside manufactured structures, particularly those with steel support structures.

At the Bioelectromagnetics Society annual meeting in 1984 [48], Blackman revealed his group's discovery that the intensity of the static magnetic field could establish and define those oscillatory frequencies that would cause changes in calcium ion release in his chick brain preparation. This result was further discussed at a NATO Advanced Research workshop in Erice, Italy in the fall of 1984 and by publications from that meeting and subsequent research: Blackman et al. [14,18] and Liboff et al. [36,49,50]. Substantial additional research on this feature was reported by Liboff and colleagues [51,52,50]. Blackman et al. also reported on the importance of the relative orientation of the static magnetic field vector to the oscillating magnetic field vector [21] and demonstrated a reverse biological response could occur depending on parallel or perpendicular orientations of the static and oscillating magnetic fields [53].

There have been many attempts to explain this phenomenon by a number of research teams led by Smith [49], Blackman [15], Liboff [36,54], Lednev [55], Blanchard [56], Zhadin [57], del Giudice [58], Binhi [59–62], and Matronchik [63] but none has been universally accepted. Nevertheless, experimental results continued to report static and oscillating field dependencies for non-thermally induced biological effects in studies led by Zhadin [64,65], Vorobyov [66], Baureus Koch [67], Sarimov [68], Prato [69,70], Comisso [71], and Novikov [72].

With this accumulation of reports from independent, international researchers, it is now clear that if a biological response depends on the static magnetic field intensity, and even its orientation with respect to an oscillating field, then the conditions necessary to reproduce the phenomenon are very specific and might easily escape detection (see for example, Blackman and Most [73]. The consequences of these results are that there may be exposure situations that are truly detrimental (or beneficial) to organisms, but that are insufficiently common on a large scale that they would not be observed in epidemiological studies; they need to be studied under controlled laboratory conditions to determine impact on health and wellbeing.

5. Electric and magnetic components—both biological active with different consequences

Both the electric and the magnetic components have been shown to directly and independently cause biological changes. There is one report that clearly distinguishes the distinct biological responses caused by the electric field and by the magnetic field. Marron et al. [74] show that electric field exposure can increase the negative surface charge density of an amoeba, Physarum polycephalum, and that magnetic field exposure of the same organism causes changes in the surface of the organism to reduce its hydrophobic character. Other scientists have used concentric growth surfaces of different radii and vertical magnetic fields perpendicular to the growth surface to determine if the magnetic or the induced electric component is the agent causing biological change. Liburdy et al. [75], examining calcium influx in lymphocytes, and Greene et al. [76], monitoring ornithine decarboxylase (ODC) activity in cell culture, showed that the induced electric component was responsible for their results. In contrast, Blackman et al. [77,78] monitoring neurite outgrowth from two different clones of PC-12 cells and using the same exposure technique used by Liburdy and by Greene showed the magnetic component was the critical agent in their experiments. EMF-induced changes on the cell surface, where it interacts with its environment, can dramatically alter the homeostatic mechanisms in tissues, whereas changes in ODC activity are associated with the induction of cell proliferation, a desirable outcome if one is concerned about wound healing, but undesirable if the concern is tumor cell growth. This information demonstrates the multiple, different ways that EMF can affect biological systems. Present analyses for risk assessment and standard setting have ignored this information, thus making their conclusions of limited value.

6. Sine and pulsed waves—like different programs on a radio broadcast station

Important characteristics of pulsed waves that have been reported to influence biological processes include the following: (1) frequency, (2) pulse width, (3) intensity, (4) rise and fall time, and (5) the frequency, if any, within the pulse ON

time. Chiabrera et al. [79] showed that pulsed fields caused de-differentiation of amphibian red blood cells. Scarfi et al. [80] showed enhanced micronuclei formation in lymphocytes of patients with Turner's syndrome (only one X chromosome) but no change in micronuclei formation when the lymphocytes were exposed to sine waves (Scarfi et al. [81]). Takahashi et al. [82] monitored thymidine incorporation in Chinese hamster cells and explored the influence of pulse frequency (two windows of enhancement reported), pulse width (one window of enhancement reported) and intensity (two windows of enhancement reported followed by a reduction in incorporation). Ubeda et al. [83] showed the influence of difference rise and fall times of pulsed waves on chick embryo development.

6.1. Importance for risk assessment

It is important to note that the frequency spectrum of pulsed waves can be represented by a sum of sine waves which, to borrow a chemical analogy, would represent a mixture of chemicals, anyone of which could be biologically active. Risk assessment and exposure limits have been established for specific chemicals or chemical classes of compounds that have been shown to cause undesirable biological effects. Risk assessors and the general public are sophisticated enough to recognize that it is impossible to declare all chemicals safe or hazardous; consider the difference between food and poisons, both of which are chemicals. A similar situation occurs for EMF; it is critical to determine which combinations of EMF conditions have the potential to cause biological harm and which do not.

Obviously, pulse wave exposures represent an entire genre of exposure conditions, with additional difficulty for exact independent replication of exposures, and thus of results, but with increased opportunities for the production of biological effects. Current standards were not developed with explicit knowledge of these additional consequences for biological responses.

7. Mechanisms

Two papers have the possibility of advancing understanding in this research area. Chiabrera et al. [84] created a theoretical model for EMF effects on an ion's interaction with protein that includes the influence of thermal energy and of metabolism. Before this publication, theoreticians assumed that biological effects in living systems could not occur if the electric signal is below the signal caused by thermal noise, in spite of experimental evidence to the contrary. In this paper, the authors show that this limitation is not absolute, and that different amounts of metabolic energy can influence the amount and parametric response of biological systems to EMF. The second paper, by Marino et al. [85], presents a new analytical approach to examine endpoints in systems exposed to EMF. The authors, focusing on exposure-induced lymphoid phenotypes, report that EMF may not cause changes in the mean values of endpoints, but by using recurrence analysis, they capture exposure-induced, statistically significant, non-linear movements of the endpoints to either side of the mean endpoint value. They provide further evidence using immunological endpoints from exposed and sham treated mice [86–88]. Additional research has emerged from this laboratory on EMF-induced animal and human brain activity changes that provides more evidence for the value of their research approach (Marino et al. [89–92], Kolomytkin et al. [93] and Carrubba et al. [94–98]). Further advanced theoretical and experimental studies of relevance to non-thermal biological effects are emerging; see for example reports by Binhi et al. [59–62], Zhadin et al. [64,99,65], and Novikov et al. [72]. *It is apparent that much remains to be examined and explained in EMF biological effects research through more creative methods of analysis than have been used before. The models described above need to be incorporated into risk assessment determinations.*

8. Problems with current risk assessments—observations of effects are segregated by artificial frequency bands that ignore modulation

One fundamental limitation of most reviews of EMF biological effects is that exposures are segregated by the physical (engineering/technical) concept of frequency bands favored by the engineering community. This is a default approach that follows the historical context established by the incremental addition of newer technologies that generate increasingly higher frequencies. However, this approach fails to consider unique responses from biological systems that are widely reported at various combinations of frequencies, modulations and intensities.

When common biological responses are observed without regard for the particular, engineering-defined EMF frequency band in which the effects occur, this reorganization of the results can highlight the commonalities in biological responses caused by exposures to EMF across the different engineering-defined frequency bands. An attempt to introduce this concept to escape the limitations of the engineering-defined structure occurred with the development of the 1986 NCRP radiofrequency exposure guidelines because published papers from the early 1970s to the mid 1980s (to be discussed below) demonstrated the need to include amplitude modulation as a factor in setting of maximum exposure limits. The 1986 NCRP guideline [1] was the one and only risk evaluation that included an exception for modulated fields.

The current research and risk assessment attempts are no longer tenable. The 3-year delay in the expected report of the 7-year Interphone study results has made this epidemiological approach a 10-year long effort, and the specific exposure conditions, due to improved technology, have changed so that the results may no longer be applicable to the current

exposure situation. It is unproductive to continue to fund epidemiological studies of people who are exposed to a wide variety of diversified, uncontrolled, and poorly characterized EMF in their natural and work environments. In place of the funding of more epidemiological studies should be funding to support controlled laboratory studies to focus on the underlying processes responsible for the NTE described above, so that mechanisms or modes of action can be developed to provide a theoretical framework to further identify, characterize and unify the action of the heretofore ignored exposure parameters shown to be important.

8.1. Potential explanation for the failure to optimize research in EMF biological effects

Unfortunately, risk evaluations following the 1986 NCRP example [1], returned to the former engineering-defined analysis conditions, in part because scientists who reported non-thermal effects were not placed on the review committees, and in the terms of Slovic [100] "Risk assessment is inherently subjective and represent a blend of science and judgment with important psychological, social, cultural, and political factors. ... Whoever controls the definition of risk controls the rational solution to the problem at hand. ... Defining risk is thus an exercise in power." It appears that by excluding scientists experienced with producing non-thermal biological effects, the usually sound judgment by the selected committees was severely limited in its breadth-of-experience, thereby causing the members to retreat to their own limited areas of expertise when forced to make judgments, as described by Slovic [100], "Public views are also influenced by worldviews, ideologies, and values; so are scientists' views, particularly when they are working at limits of their expertise." The current practice of segregating scientific investigations (and resulting public health limits) by artificial divisions of frequency dramatically dilutes the impact of the basic science results, thereby reducing and distorting the weight of evidence in any evaluation process (see evaluations of bias by Havas [101], referring to NRC 1997 [102] compared to NIEHS 1998 [103] and NIEHS 1999 [104]).

9. Suggested research

Are there substitute approaches that would improve on the health-effects evaluation situation? As mentioned above, it may be useful in certain cases to develop a biologically based clustering of the data to focus on and enrich understanding of certain aspects of biological responses. Some examples to consider for biological clustering include: (1) EMF features, such as frequency and intensity inter-dependencies, (2) common co-factors, such as the earth's magnetic field or co-incident application of chemical agents to perturb and perhaps sensitize the biological system to EMF, or (3) physiological state of the biological specimen, such as age or sensitive sub-populations, including genetic predisposition as described by Fedrowitz et al. [105,106], and for human populations, recently reported by Yang et al. [107].

To determine if this approach has merit, one could combine reports of biological effects found in the ELF (including sub-ELF) band with effects found in the RF band when the RF exposures are amplitude modulated (AM) using frequencies in the ELF band. The following data should be used: (a) human response time changes under ELF exposure [2], (b) monkey response time and EEG changes under ELF exposure [3,4], (c) cat brain EEG, GABA and calcium ion changes induced by ELF and AM-RF [8,9,7,10,6,11,108,5], (d) calcium ion changes in chick brain tissue under ELF and AM-RF [8,9,7,10,13–15,21,16–18,12,19,20,22,35,23–25,11], and (e) calcium changes under AM-RF in brain cells in culture [26–28] and in frog heart under AM-RF [31]. The potential usefulness of applying biological clustering in the example given above even though AM is used, is that the results may have relevance to assist in the examination of some of the effects reportedly caused by cellular phone exposures which include more complex types of modulation of RF. This suggestion is reasonable because three groups later reported human responses to cell phone emissions that include changes in reaction times – Preece et al. [109,110], Koivisto et al. [111,112] and Krause et al. [113,114] – or to brain wave potentials that may be associated with reaction time changes—Freude et al. [115,116].

Subsequently, Preece et al. [117] tested cognitive function in children and found a trend, but not a statistically significant change in simple reaction time under exposure, perhaps because he applied a Bonferroni correction to his data (alpha for significance was required to be less than 0.0023). It would appear that a change in the experimental protocol might provide a more definitive test of the influence of exposure on simple reaction time because it is known that a Bonferroni correction is a particularly severe test of statistical significance, or as the author observed, "a particularly conservative criterion."

Krause et al. [118] examined cognitive activity by observing oscillatory EEG activity in children exposed to cell phone radiation while performing an auditory memory task and reported exposure related changes in the ~4–8 Hz EEG frequencies during memory encoding, and changes in that range and also ~15 Hz during recognition. The investigators also examined cognitive processing, an auditory memory task or a visual working memory task, in adults exposed to CW or pulsed cell phone radiation on either the right or left side of the head, and reported modest changes in brain EEG activity in the ~4–8 Hz region, compared to CW exposure, but with caveats that no behavior changes were observed, and that the data were varying, unsystematic and inconsistent with previous reports (Krause et al. [119]). Haarala and colleagues conducted an extensive series of experiments, examining reaction time [120], short-term memory [121], short-term memory in children [122], and right versus left hemisphere exposure [123]. Although these studies did not

support the positive effects from exposure reported by others, they provided possible explanations for the apparent lack of agreement.

Other research groups have also examined the effects of cell phone radiation on the central nervous system, including Borbely et al. [124], Huber et al. [125], Loughran et al. [126], and D'Costa et al. [127], who found changes in sleep EEG patterns and other measures during or after short-term exposures, while others, such as Fritzer et al. [128] exposed for longer time periods found no changes in sleep parameters, EEG power spectra, correlation dimension nor cognitive function. The work of Pritchard [129] served as the basis to examining correlation dimensions, which is opening a potentially fertile avenue for investigation. Although this approach provides more indepth information on ongoing processes and function, it has not yet been used to address potential consequences associated with long-term cell phone use.

The papers published in the 1960s through 1991, described in earlier sections of this paper, foreshadowed the more recent publications in 1999 through 2008 showing response time changes, or associated measures, in human subjects during exposure to cell phone-generated radiation. It is unfortunate that essentially none of the earlier studies was acknowledged in these recent reports on cognition, reaction time and other measures of central nervous system processes. Without guidance from this extensive earlier work, particularly those demonstrating the variety of exposure parameter spaces that must be controlled to produce repeatable experiments, the development of the mechanistic bases for non-thermal effects from EMF exposures will be substantially delayed. The omission of the recognition of the exposure conditions that affect the biological outcomes continues as recently as the National Academy of Science 2009 publication [130] of future directions for research, which emphasizes the modest perspective in the results from committee members working at the limits of expertise, as anticipated by Slovic [100].

Let us hope that subsequent national and international committees that consider future directions for EMF research include members who have performed and reported non-thermal effects, in order to provide a broader perspective to develop programs that will more expeditiously address potential health problems as well as to provide guidance to industry on prudent procedures to establish for their technologies.

At present, we are left with a recommendation voiced in 1989 by Abelson [131] in an editorial in Science Magazine that addressed electric power-specific EMF, but is applicable to higher frequency EMF as well, to "adopt a prudent avoidance strategy" by "adopting those which look to be 'prudent' investments given their cost and our current level of scientific understanding about possible risks."

10. Conclusions

There is substantial scientific evidence that some modulated fields (pulsed or repeated signals) are bioactive, which increases the likelihood that they could have health impacts with chronic exposure even at very low exposure levels. Modulation signals may interfere with normal, non-linear biological processes. Modulation is a fundamental factor that should be taken into account in new public safety standards; at present it is not even a contributing factor. To properly evaluate the biological and health impacts of exposure to modulated RFR (carrier waves), it is also essential to study the impact of the modulating signal (lower frequency fields or ELF-modulated RF). Current standards have ignored modulation as a factor in human health impacts, and thus are inadequate in the protection of the public in terms of chronic exposure to some forms of ELF-modulated RF signals. The current IEEE and ICNIRP standards are not sufficiently protective of public health with respect to chronic exposure to modulated fields (particularly new technologies that are pulse-modulated and heavily used in cellular telephony). The collective papers on modulation appear to be omitted from consideration in the recent WHO and IEEE science reviews. This body of research has been ignored by current standard setting bodies that rely only on traditional energy-based (thermal) concepts. More laboratory as opposed to epidemiological research is needed to determine which modulation factors, and combinations are bioactive and deleterious at low intensities, and are likely to result in disease-related processes and/or health risks; however this should not delay preventative actions supporting public health and wellness. If signals need to be modulated in the development of new wireless technologies, for example, it makes sense to use what existing scientific information is available to avoid the most obviously deleterious exposure parameters and select others that may be less likely to interfere with normal biological processes in life. The current membership on Risk Assessment committees needs to be made more inclusive, by adding scientists experienced with producing non-thermal biological effects. The current practice of segregating scientific investigations (and resulting public health limits) by artificial, engineering-based divisions of frequency needs to be changed because this approach dramatically dilutes the impact of the basic science results and eliminates consideration of modulation signals, thereby reducing and distorting the weight of evidence in any evaluation process.

References

[1] National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.

[2] J. Hamer, Effects of low level, low frequency electric fields on human reaction time, Communications in Behavioral Biology 2 (5 part A) (1968) 217–222.

[3] R.J. Gavalas, D.O. Walter, J. Hamer, W.R. Adey, Effect of low-level, low-frequency electric fields on eeg and behavior in macaca nemestrina, Brain Research 18 (3) (1970) 491–501.

[4] R. Gavalas-Medici, S.R. Day-Magdaleno, Extremely low frequency, weak electric fields affect schedule-controlled behaviour of monkeys, Nature 261 (5557) (1976) 256–259.

[5] L.K. Kaczmarek, W.R. Adey, The efflux of 45ca2+ and (3 h)gamma-aminobutyric acid from cate cerebral cortex, Brain Research 63 (1973) 331–342.

[6] L.K. Kaczmarek, W.R. Adey, Weak electric gradients change ionic and transmitter fluxes in cortex, Brain Research 66 (3) (1974) 537–540.

[7] S.M. Bawin, L.K. Kaczmarek, W.R. Adey, Effects of modulated vhf fields on the central nervous system, Annals of the New York Academy of Sciences 247 (1975) 74–81.

[8] S.M. Bawin, W.R. Adey, Sensitivity of calcium binding in cerebral tissue to weak environmental electric fields oscillating at low frequency, Proceedings of the National Academy of Sciences of the United States of America 73 (6) (1976) 1999–2003.

[9] S.M. Bawin, W.R. Adey, I.M. Sabbot, Ionic factors in release of 45ca2+ from chicken cerebral tissue by electromagnetic fields, Proceedings of the National Academy of Sciences of the United States of America 75 (12) (1978) 6314–6318.

[10] S.M. Bawin, A.R. Sheppard, W.R. Adey, Possible mechanism of weak electromagnetic field coupling in brain tissue, Bioelectrochemistry & Bioenergetics 5 (1978) 67–76.

[11] A.R. Sheppard, S.M. Bawin, W.R. Adey, Models of long-range order in cerebral macromolecules: effects of sub-elf and of modulated vhf and uhf fields, Radio Science 14 (6S) (1979) 141–145.

[12] C.F. Blackman, J.A. Elder, C.M. Weil, S.G. Benane, D.C. Eichinger, D.E. House, Induction of calcium ion efflux from brain tissue by radio-frequency radiation: effects of modulation-frequency and field strength, Radio Science 14 (6S) (1979) 93–98.

[13] C.F. Blackman, S.G. Benane, J.A. Elder, D.E. House, J.A. Lampe, J.M. Faulk, Induction of calcium-ion efflux from brain tissue by radiofrequency radiation: effect of sample number and modulation frequency on the power-density window, Bioelectromagnetics 1 (1) (1980) 35–43.

[14] C.F. Blackman, The biological influences of low-frequency sinusoidal electromagnetic signals alone and superimposed on rf carrier waves; in: A. Chiabrera, C. Nicolini, H.P. Schwan (Eds.), Interaction between Electromagnetic Fields and Cells, Erice, Italy, Plenum, New York, 1984, NATO ASI Series A97, pp. 521–535.

[15] C.F. Blackman, S.G. Benane, D.J. Elliott, D.E. House, M.M. Pollock, Influence of electromagnetic fields on the efflux of calcium ions from brain tissue in vitro: a three-model analysis consistent with the frequency response up to 510 hz, Bioelectromagnetics 9 (3) (1988) 215–227.

[16] C.F. Blackman, S.G. Benane, W.T. Joines, M.A. Hollis, D.E. House, Calcium-ion efflux from brain tissue: power-density versus internal field-intensity dependencies at 50-mhz rf radiation, Bioelectromagnetics 1 (3) (1980) 277–283.

[17] C.F. Blackman, S.G. Benane, L.S. Kinney, W.T. Joines, D.E. House, Effects of elf fields on calcium-ion efflux from brain tissue in vitro, Radiation Research 92 (3) (1982) 510–520.

[18] C.F. Blackman, S.G. Benane, J.R. Rabinowitz, D.E. House, W.T. Joines, A role for the magnetic field in the radiation-induced efflux of calcium ions from brain tissue in vitro, Bioelectromagnetics 6 (4) (1985) 327–337.

[19] C.F. Blackman, D.E. House, S.G. Benane, W.T. Joines, R.J. Spiegel, Effect of ambient levels of power-line-frequency electric fields on a developing vertebrate, Bioelectromagnetics 9 (2) (1988) 129–140.

[20] C.F. Blackman, W.T. Joines, J.A. Elder, Calcium-ion efflux in brain tissue by radiofrequency radiation;, in: K.H. Illinger (Ed.), Biological Effects of Nonionizing Radiation, vol. 157, American Chemical Society, Washington, DC, 1981, pp. 299–314.

[21] C.F. Blackman, S.G. Benane, D.E. House, D.J. Elliott, Importance of alignment between local dc magnetic field and an oscillating magnetic field in responses of brain tissue in vitro and in vivo, Bioelectromagnetics 11 (2) (1990) 159–167.

[22] C.F. Blackman, L.S. Kinney, D.E. House, W.T. Joines, Multiple power-density windows and their possible origin, Bioelectromagnetics 10 (2) (1989) 115–128.

[23] W.T. Joines, C.F. Blackman, Equalizing the electric field intensity within chick brain immersed in buffer solution at different carrier frequencies, Bioelectromagnetics 2 (4) (1981) 411–413.

[24] W.T. Joines, C.F. Blackman, M.A. Hollis, Broadening of the rf power-density window for calcium-ion efflux from brain tissue, IEEE Transactions on Bio-Medical Engineering 28 (8) (1981) 568–573.

[25] W.T. Joines, C.F. Blackman, R.J. Spiegel, Specific absorption rate in electrically coupled biological samples between metal plates, Bioelectromagnetics 7 (2) (1986) 163–176.

[26] S.K. Dutta, K. Das, B. Ghosh, C.F. Blackman, Dose dependence of acetylcholinesterase activity in neuroblastoma cells exposed to modulated radio-frequency electromagnetic radiation, Bioelectromagnetics 13 (4) (1992) 317–322.

[27] S.K. Dutta, B. Ghosh, C.F. Blackman, Radiofrequency radiation-induced calcium ion efflux enhancement from human and other neuroblastoma cells in culture, Bioelectromagnetics 10 (2) (1989) 197–202.

[28] S.K. Dutta, A. Subramoniam, B. Ghosh, R. Parshad, Microwave radiation-induced calcium ion efflux from human neuroblastoma cells in culture, Bioelectromagnetics 5 (1) (1984) 71–78.

[29] S.K. Dutta, M. Verma, C.F. Blackman, Frequency-dependent alterations in enolase activity in escherichia coli caused by exposure to electric and magnetic fields, Bioelectromagnetics 15 (5) (1994) 377–383.

[30] E. Albert, C. Blackman, F. Slaby, Calcium dependent secretory protein release and calcium efflux during rf irradiation of rat pancreatic tissue slices, in: A.J. Berteaud, B. Servantie (Eds.), Ondes Electromagnetiques et Biologie, URSI International Symposium on Electromagnetic Waves and Biology, June 30–July 4. Jouy-en-Josas, France, Centre National de la Recherche Scientifique, 2 rue Henry Dunant, 94320 Thiais, France: A.J. Berteaud, 1980, pp. 325–329.

[31] J.L. Schwartz, D.E. House, G.A. Mealing, Exposure of frog hearts to cw or amplitude-modulated vhf fields: selective efflux of calcium ions at 16 hz, Bioelectromagnetics 11 (4) (1990) 349–358.

[32] J.L. Schwartz, G.A. Mealing, Calcium-ion movement and contractility in atrial strips of frog heart are not affected by low-frequency-modulated, 1 ghz electromagnetic radiation, Bioelectromagnetics 14 (6) (1993) 521–533.

[33] C.F. Blackman, Can EMF exposure during development leave an imprint later in life? Electromagnetic Biology and Medicine 25 (4) (2006) 217–225.

[34] C.J. Thompson, Y.S. Yang, V. Anderson, A.W. Wood, A cooperative model for ca(++) efflux windowing from cell membranes exposed to electromagnetic radiation, Bioelectromagnetics 21 (6) (2000) 455–464.

[35] W.T. Joines, C.F. Blackman, Power density, field intensity, and carrier frequency determinants of rf-energy-induced calcium-ion efflux from brain tissue, Bioelectromagnetics 1 (3) (1980) 271–275.

[36] A.R. Liboff, Cyclotron resonance in membrane transport, in: A. Chiabrera, C. Nicolini, H.P. Schwan (Eds.), Interaction Between Electromagnetic Fields and Cells, Erice, Italy, Plenum, New York, 1984, NATO ASI Series A97, pp. 281–296.

[37] T.A. Litovitz, D. Krause, C.J. Montrose, J.M. Mullins, Temporally incoherent magnetic fields mitigate the response of biological systems to temporally coherent magnetic fields, Bioelectromagnetics 15 (5) (1994) 399–409.

[38] J.M. Farrell, M. Barber, D. Krause, T.A. Litovitz, The superposition of a temporally incoherent magnetic field inhibits 60 hz-induced changes in the odc activity of developing chick embryos, Bioelectromagnetics 19 (1) (1998) 53–56.

[39] T.A. Litovitz, C.J. Montrose, P. Doinov, K.M. Brown, M. Barber, Superimposing spatially coherent electromagnetic noise inhibits field-induced abnormalities in developing chick embryos, Bioelectromagnetics 15 (2) (1994) 105–113.

[40] T.A. Litovitz, L.M. Penafiel, J.M. Farrel, D. Krause, R. Meister, J.M. Mullins, Bioeffects induced by exposure to microwaves are mitigated by superposition of elf noise, Bioelectromagnetics 18 (6) (1997) 422–430.

[41] S. Milham, L.L. Morgan, A new electromagnetic exposure metric: high frequency voltage transients associated with increased cancer incidence in teachers in a california school, American Journal of Industrial Medicine 51 (8) (2008) 579–586.

[42] M. Havas, Electromagnetic hypersensitivity: biological effects of dirty electricity with emphasis on diabetes and multiple sclerosis, Electromagnetic Biology and Medicine 25 (4) (2006) 259–268.

[43] M. Havas, Dirty electricity elevates blood sugar among electrically sensitive diabetics and may explain brittle diabetes, Electromagnetic Biology and Medicine 27 (2) (2008) 135–146.

[44] M. Havas, A. Olstad, Power quality affects teacher wellbeing and student behavior in three Minnesota schools, The Science of the Total Environment 402 (2–3) (2008) 157–162.

[45] C.F. Blackman, S.G. Benane, D.E. House, Frequency-dependent interference by magnetic fields of nerve growth factor-induced neurite outgrowth in pc-12 cells, Bioelectromagnetics 16 (6) (1995) 387–395.

[46] C.F. Blackman, J.P. Blanchard, S.G. Benane, D.E. House, Experimental determination of hydrogen bandwidth for the ion parametric resonance model, Bioelectromagnetics 20 (1) (1999) 5–12.

[47] M.A. Trillo, A. Ubeda, J.P. Blanchard, D.E. House, C.F. Blackman, Magnetic fields at resonant conditions for the hydrogen ion affect neurite outgrowth in pc-12 cells: a test of the ion parametric resonance model, Bioelectromagnetics 17 (1) (1996) 10–20.

[48] L. Slesin, Highlights: Elf bioeffects studies at bems, Microwave News IV (7, Sept.) (1984) 2.

[49] S.D. Smith, B.R. McLeod, A.R. Liboff, K. Cooksey, Calcium cyclotron resonance and diatom mobility, Bioelectromagnetics 8 (3) (1987) 215–227.

[50] J.R. Thomas, J. Schrot, A.R. Liboff, Low-intensity magnetic fields alter operant behavior in rats, Bioelectromagnetics 7 (4) (1986) 349–357.

[51] A.R. Liboff, B.R. McLeod, Kinetics of channelized membrane ions in magnetic fields, Bioelectromagnetics 9 (1) (1988) 39–51.

[52] A.R. Liboff, W.C. Parkinson, Search for ion-cyclotron resonance in an na(+)-transport system, Bioelectromagnetics 12 (2) (1991) 77–83.

[53] C.F. Blackman, J.P. Blanchard, S.G. Benane, D.E. House, Effect of ac and dc magnetic field orientation on nerve cells, Biochemical and Biophysical Research Communications 220 (3) (1996) 807–811.

[54] A.R. Liboff, Electric-field ion cyclotron resonance, Bioelectromagnetics 18 (1) (1997) 85–87.

[55] V.V. Lednev, Possible mechanism for the influence of weak magnetic fields on biological systems, Bioelectromagnetics 12 (2) (1991) 71–75.

[56] J.P. Blanchard, C.F. Blackman, Clarification and application of an ion parametric resonance model for magnetic field interactions with biological systems, Bioelectromagnetics 15 (3) (1994) 217–238.

[57] M.N. Zhadin, E.E. Fesenko, Ionic cyclotron resonance in biomolecules, Biomedical Science 1 (3) (1990) 245–250.

[58] E. Del Giudice, M. Fleischmann, G. Preparata, G. Talpo, On the "Unreasonable" Effects of elf magnetic fields upon a system of ions, Bioelectromagnetics 23 (7) (2002) 522–530.

[59] V.N. Binhi, Stochastic dynamics of magnetosomes and a mechanism of biological orientation in the geomagnetic field, Bioelectromagnetics 27 (1) (2006) 58–63.

[60] V.N. Binhi, A few remarks on 'combined action of dc and ac magnetic fields on ion motion in a macromolecule', Bioelectromagnetics 28 (5) (2007) 409–412, discussion 412–404.

[61] V.N. Binhi, A.B. Rubin, Magnetobiology: the kt paradox and possible solutions, Electromagnetic Biology and Medicine 26 (1) (2007) 45–62.

[62] V.N. Binhi, A.V. Savin, Molecular gyroscopes and biological effects of weak extremely low-frequency magnetic fields, Physical Review 65 (5 Pt 1) (2002) 051912.

[63] A.Y. Matronchik, I.Y. Belyaev, Mechanism for combined action of microwaves and static magnetic field: slow non uniform rotation of charged nucleoid, Electromagnetic Biology and Medicine 27 (4) (2008) 340–354.

[64] M.N. Zhadin, Combined action of static and alternating magnetic fields on ion motion in a macromolecule: theoretical aspects, Bioelectromagnetics 19 (5) (1998) 279–292.

[65] M.N. Zhadin, V.V. Novikov, F.S. Barnes, N.F. Pergola, Combined action of static and alternating magnetic fields on ionic current in aqueous glutamic acid solution, Bioelectromagnetics 19 (1) (1998) 41–45.

[66] V.V. Vorobyov, E.A. Sosunov, N.I. Kukushkin, V.V. Lednev, Weak combined magnetic field affects basic and morphine-induced rat's eeg, Brain Research 781 (1–2) (1998) 182–187.

[67] C.L. Baureus Koch, M. Sommarin, B.R. Persson, L.G. Salford, J.L. Eberhardt, Interaction between weak low frequency magnetic fields and cell membranes, Bioelectromagnetics 24 (6) (2003) 395–402.

[68] R. Sarimov, E. Markova, F. Johansson, D. Jenssen, I. Belyaev, Exposure to elf magnetic field tuned to zn inhibits growth of cancer cells, Bioelectromagnetics 26 (8) (2005) 631–638.

[69] F.S. Prato, M. Kavaliers, J.J. Carson, Behavioural evidence that magnetic field effects in the land snail, cepaea nemoralis, might not depend on magnetite or induced electric currents, Bioelectromagnetics 17 (2) (1996) 123–130.

[70] F.S. Prato, M. Kavaliers, A.P. Cullen, A.W. Thomas, Light-dependent and -independent behavioral effects of extremely low frequency magnetic fields in a land snail are consistent with a parametric resonance mechanism, Bioelectromagnetics 18 (3) (1997) 284–291.

[71] N. Comisso, E. Del Giudice, A. De Ninno, M. Fleischmann, L. Giuliani, G. Mengoli, F. Merlo, G. Talpo, Dynamics of the ion cyclotron resonance effect on amino acids adsorbed at the interfaces, Bioelectromagnetics 27 (1) (2006) 16–25.

[72] V.V. Novikov, I.M. Sheiman, E.E. Fesenko, Effect of weak static and low-frequency alternating magnetic fields on the fission and regeneration of the planarian dugesia (girardia) tigrina, Bioelectromagnetics 29 (5) (2008) 387–393.

[73] C.F. Blackman, B. Most, A scheme for incorporating dc magnetic fields into epidemiological studies of EMF exposure, Bioelectromagnetics 14 (5) (1993) 413–431.

[74] M.T. Marron, E.M. Goodman, P.T. Sharpe, B. Greenebaum, Low frequency electric and magnetic fields have different effects on the cell surface, FEBS Letters 230 (1–2) (1988) 13–16.

[75] R.P. Liburdy, Calcium signaling in lymphocytes and elf fields. Evidence for an electric field metric and a site of interaction involving the calcium ion channel, FEBS Letters 301 (1) (1992) 53–59.

[76] J.J. Greene, W.J. Skowronski, J.M. Mullins, R.M. Nardone, M. Penafiel, R. Meister, Delineation of electric and magnetic field effects of extremely low frequency electromagnetic radiation on transcription, Biochemical and Biophysical Research Communications 174 (2) (1991) 742–749.

[77] C.F. Blackman, S.G. Benane, D.E. House, Evidence for direct effect of magnetic fields on neurite outgrowth, FASEB J 7 (9) (1993) 801–806.

[78] C.F. Blackman, S.G. Benane, D.E. House, M.M. Pollock, Action of 50 hz magnetic fields on neurite outgrowth in pheochromocytoma cells, Bioelectromagnetics 14 (3) (1993) 273–286.

[79] A. Chiabrera, M. Hinsenkamp, A.A. Pilla, J. Ryaby, D. Ponta, A. Belmont, F. Beltrame, M. Grattarola, C. Nicolini, Cytofluorometry of electromagnetically controlled cell dedifferentiation, The Journal of Histochemistry and Cytochemistry 27 (1) (1979) 375–381.

[80] M.R. Scarfi, F. Prisco, M.B. Lioi, O. Zeni, M. Della Noce, R. Di Pietro, C. Fanceschi, D. Iafusco, M. Motta, B. F., Cytogenetic effects induced by extremely low frequency pulsed magnetic fields in lymphocytes from Turner's syndrome subjects, Bioelectrochemistry & Bioenergetics 43 (1997) 221–226.

[81] M.R. Scarfi, M.B. Lioi, O. Zeni, G. Franceschetti, C. Franceschi, F. Bersani, Lack of chromosomal aberration and micronucleus induction

in human lymphocytes exposed to pulsed magnetic fields, Mutation Research 306 (2) (1994) 129–133.

[82] K. Takahashi, I. Kaneko, M. Date, E. Fukada, Effect of pulsing electromagnetic fields on DNA synthesis in mammalian cells in culture, Experientia 42 (2) (1986) 185–186.

[83] A. Ubeda, J. Leal, M.A. Trillo, M.A. Jimenez, J.M. Delgado, Pulse shape of magnetic fields influences chick embryogenesis, Journal of Anatomy 137 (Pt 3) (1983) 513–536.

[84] A. Chiabrera, B. Bianco, E. Moggia, J.J. Kaufman, Zeeman-stark modeling of the rf EMF interaction with ligand binding, Bioelectromagnetics 21 (4) (2000) 312–324.

[85] A.A. Marino, R.M. Wolcott, R. Chervenak, F. Jourd'Heuil, E. Nilsen, C. Frilot 2nd, Nonlinear response of the immune system to power-frequency magnetic fields, American Journal of Physiology 279 (3) (2000) R761–768.

[86] A.A. Marino, R.M. Wolcott, R. Chervenak, F. Jourd'heuil, E. Nilsen, C. Frilot 2nd, Nonlinear determinism in the immune system. In vivo influence of electromagnetic fields on different functions of murine lymphocyte subpopulations, Immunological Investigations 30 (4) (2001) 313–334.

[87] A.A. Marino, R.M. Wolcott, R. Chervenak, F. Jourd'heuil, E. Nilsen, C. Frilot 2nd, Nonlinear dynamical law governs magnetic field induced changes in lymphoid phenotype, Bioelectromagnetics 22 (8) (2001) 529–546.

[88] A.A. Marino, R.M. Wolcott, R. Chervenak, F. Jourd'heuil, E. Nilsen, C. Frilot 2nd, S.B. Pruett, Coincident nonlinear changes in the endocrine and immune systems due to low-frequency magnetic fields, Neuroimmunomodulation 9 (2) (2001) 65–77.

[89] A.A. Marino, E. Nilsen, A.L. Chesson Jr., C. Frilot, Effect of low-frequency magnetic fields on brain electrical activity in human subjects, Clinical Neurophysiology 115 (5) (2004) 1195–1201.

[90] A.A. Marino, E. Nilsen, C. Frilot, Localization of electroreceptive function in rabbits, Physiology & Behavior 79 (4–5) (2003) 803–810.

[91] A.A. Marino, E. Nilsen, C. Frilot, Nonlinear changes in brain electrical activity due to cell phone radiation, Bioelectromagnetics 24 (5) (2003) 339–346.

[92] A.A. Marino, E. Nilsen, C. Frilot, Consistent magnetic-field induced dynamical changes in rabbit brain activity detected by recurrence quantification analysis, Brain Research 964 (2) (2003) 317–326.

[93] O.V. Kolomytkin, S. Dunn, F.X. Hart, C. Frilot 2nd, D. Kolomytkin, A.A. Marino, Glycoproteins bound to ion channels mediate detection of electric fields: a proposed mechanism and supporting evidence, Bioelectromagnetics 28 (5) (2007) 379–385.

[94] S. Carrubba, C. Frilot, A. Chesson, A.A. Marino, Detection of nonlinear event-related potentials, Journal of Neuroscience Methods 157 (1) (2006) 39–47.

[95] S. Carrubba, C. Frilot, A.L. Chesson, A.A. Marino, Nonlinear eeg activation evoked by low-strength low-frequency magnetic fields, Neuroscience Letters 417 (2) (2007) 212–216.

[96] S. Carrubba, C. Frilot 2nd, A.L. Chesson Jr., A.A. Marino, Evidence of a nonlinear human magnetic sense, Neuroscience 144 (1) (2007) 356–367.

[97] S. Carrubba, C. Frilot, A.L. Chesson Jr., A.A. Marino, Method for detection of changes in the eeg induced by the presence of sensory stimuli, Journal of Neuroscience Methods 173 (1) (2008) 41–46.

[98] S. Carrubba, C. Frilot, A.L. Chesson Jr., C.L. Webber Jr., J.P. Zbilut, A.A. Marino, Magnetosensory evoked potentials: consistent nonlinear phenomena, Neuroscience Research 60 (1) (2008) 95–105.

[99] M.N. Zhadin, O.N. Deryugina, T.M. Pisachenko, Influence of combined dc and ac magnetic fields on rat behavior, Bioelectromagnetics 20 (6) (1999) 378–386.

[100] P. Slovic, Trust, emotion, sex, politics, and science: surveying the risk-assessment battlefield, Risk Analysis 19 (4) (1999) 689–701.

[101] M. Havas, Biological effects of non-ionizing electromagnetic energy: a critical review of the reports by the US national research council and the us national institute of environmental health sciences as they relate to the broad realm of EMF bioeffects, Environmental Reviews 8 (2000) 173–253.

[102] National Research Council (U.S.), Committee on the Possible Effects of Electromagnetic Fields on Biologic Systems, National Academy Press, Washington, DC, 1997, 356 pp.

[103] National Institute of Environmental Health Science Working Group Report, Assessment of health effects from exposure to power-line frequencyelectric and magnetic fields, 1998, NIH Pub 98-3981, 508 pp.

[104] National Institute of Environmental Health Science, Report on health effects from exposure to power-line frequency electric and magnetic fields, NIH Pub No 99-4493, 1999, 67 pp.

[105] M. Fedrowitz, K. Kamino, W. Loscher, Significant differences in the effects of magnetic field exposure on 7, 12-dimethylbenz(a)anthracene-induced mammary carcinogenesis in two substrains of sprague-dawley rats, Cancer Research 64 (1) (2004) 243–251.

[106] M. Fedrowitz, W. Loscher, Power frequency magnetic fields increase cell proliferation in the mammary gland of female fischer 344 rats but not various other rat strains or substrains, Oncology 69 (6) (2005) 486–498.

[107] Y. Yang, X. Jin, C. Yan, Y. Tian, J. Tang, X. Shen, Case-only study of interactions between DNA repair genes (hmlh1, apex1, mgmt, xrcc1 and xpd) and low-frequency electromagnetic fields in childhood acute leukemia, Leukemia & Lymphoma 49 (12) (2008) 2344–2350.

[108] S.M. Bawin, R.J. Gavalas-Medici, W.R. Adey, Effects of modulated very high frequency fields on specific brain rhythms in cats, Brain Research 58 (2) (1973) 365–384.

[109] A.W. Preece, G. Iwi, A. Davies-Smith, K. Wesnes, S. Butler, E. Lim, A. Varey, Effect of a 915-mhz simulated mobile phone signal on cognitive function in man, International Journal of Radiation Biology 75 (4) (1999) 447–456.

[110] A.W. Preece, K.A. Wesnes, G.R. Iwi, The effect of a 50 hz magnetic field on cognitive function in humans, International Journal of Radiation Biology 74 (4) (1998) 463–470.

[111] M. Koivisto, C.M. Krause, A. Revonsuo, M. Laine, H. Hamalainen, The effects of electromagnetic field emitted by gsm phones on working memory, Neuroreport 11 (8) (2000) 1641–1643.

[112] M. Koivisto, A. Revonsuo, C. Krause, C. Haarala, L. Sillanmaki, M. Laine, H. Hamalainen, Effects of 902 mhz electromagnetic field emitted by cellular telephones on response times in humans, Neuroreport 11 (2) (2000) 413–415.

[113] C.M. Krause, L. Sillanmaki, M. Koivisto, A. Haggqvist, C. Saarela, A. Revonsuo, M. Laine, H. Hamalainen, Effects of electromagnetic field emitted by cellular phones on the eeg during a memory task, Neuroreport 11 (4) (2000) 761–764.

[114] C.M. Krause, L. Sillanmaki, M. Koivisto, A. Haggqvist, C. Saarela, A. Revonsuo, M. Laine, H. Hamalainen, Effects of electromagnetic fields emitted by cellular phones on the electroencephalogram during a visual working memory task, International Journal of Radiation Biology 76 (12) (2000) 1659–1667.

[115] G. Freude, P. Ullsperger, S. Eggert, I. Ruppe, Effects of microwaves emitted by cellular phones on human slow brain potentials, Bioelectromagnetics 19 (6) (1998) 384–387.

[116] G. Freude, P. Ullsperger, S. Eggert, I. Ruppe, Microwaves emitted by cellular telephones affect human slow brain potentials, European journal of Applied Physiology 81 (1–2) (2000) 18–27.

[117] A.W. Preece, S. Goodfellow, M.G. Wright, S.R. Butler, E.J. Dunn, Y. Johnson, T.C. Manktelow, K. Wesnes, Effect of 902 mhz mobile phone transmission on cognitive function in children, Bioelectromagnetics (Suppl. 7) (2005) S138–143.

[118] C.M. Krause, C.H. Bjornberg, M. Pesonen, A. Hulten, T. Liesivuori, M. Koivisto, A. Revonsuo, M. Laine, H. Hamalainen, Mobile phone effects on children's event-related oscillatory eeg during an auditory memory task, International Journal of Radiation Biology 82 (6) (2006) 443–450.

[119] C.M. Krause, M. Pesonen, C. Haarala Bjornberg, H. Hamalainen, Effects of pulsed and continuous wave 902 mhz mobile phone exposure on brain oscillatory activity during cognitive processing, Bioelectromagnetics 28 (4) (2007) 296–308.

[120] C. Haarala, L. Bjornberg, M. Ek, M. Laine, A. Revonsuo, M. Koivisto, H. Hamalainen, Effect of a 902 mhz electromagnetic field emitted by mobile phones on human cognitive function: a replication study, Bioelectromagnetics 24 (4) (2003) 283–288.

[121] C. Haarala, M. Ek, L. Bjornberg, M. Laine, A. Revonsuo, M. Koivisto, H. Hamalainen, 902 mhz mobile phone does not affect short term memory in humans, Bioelectromagnetics 25 (6) (2004) 452–456.

[122] C. Haarala, M. Bergman, M. Laine, A. Revonsuo, M. Koivisto, H. Hamalainen, Electromagnetic field emitted by 902 mhz mobile phones shows no effects on children's cognitive function, Bioelectromagnetics Suppl. 7 (2005) S144–150.

[123] C. Haarala, F. Takio, T. Rintee, M. Laine, M. Koivisto, A. Revonsuo, H. Hamalainen, Pulsed and continuous wave mobile phone exposure over left versus right hemisphere: effects on human cognitive function, Bioelectromagnetics 28 (4) (2007) 289–295.

[124] A.A. Borbely, R. Huber, T. Graf, B. Fuchs, E. Gallmann, P. Achermann, Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram, Neuroscience Letters 275 (3) (1999) 207–210.

[125] R. Huber, J. Schuderer, T. Graf, K. Jutz, A.A. Borbely, N. Kuster, P. Achermann, Radio frequency electromagnetic field exposure in humans: estimation of sar distribution in the brain, effects on sleep and heart rate, Bioelectromagnetics 24 (4) (2003) 262–276.

[126] S.P. Loughran, A.W. Wood, J.M. Barton, R.J. Croft, B. Thompson, C. Stough, The effect of electromagnetic fields emitted by mobile phones on human sleep, Neuroreport 16 (17) (2005) 1973–1976.

[127] H. D'Costa, G. Truemann, L. Tang, U. Abdel-rahman, W. Abdel-rahman, K. Ong, I. Cosic, Human brain wave activity during exposure to radiofrequency field emissions from mobile phones, Australasian Physical & Engineering Sciences in Medicine 26 (2003) 162–167.

[128] G. Fritzer, R. Goder, L. Friege, J. Wachter, V. Hansen, D. Hinze-Selch, J.B. Aldenhoff, Effects of short- and long-term pulsed radiofrequency electromagnetic fields on night sleep and cognitive functions in healthy subjects, Bioelectromagnetics 28 (4) (2007) 316–325.

[129] W.S. Pritchard, D.W. Duke, Measuring chaos in the brain: a tutorial review of nonlinear dynamical eeg analysis, The International Journal of Neuroscience 67 (1–4) (1992) 31–80.

[130] National Academy of Science, Identification of Research Needs Relating to Potential Biological or Adverse Health Effects of Wireless Communication, Washington, DC, 2009, http//www.nap.edu/catalog/12036.html.

[131] P.H. Abelson, Effects of electric and magnetic fields, Science (New York, N.Y.) 245 (4915) (1989) 241.

ELSEVIER

Pathophysiology 16 (2009) 217–231

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Late Lessons from Early Warnings: Towards realism and precaution with EMF?

David Gee *

European Environment Agency, Kongens Nytorv 6, DK-1050 Copenhagen K, Denmark

Received 17 December 2008; accepted 30 January 2009

Abstract

The histories of some well-known public and environmental hazards, from the first scientifically based early warnings about potential harm, to the subsequent precautionary and preventive measures, have been reviewed by the European Environment Agency in their report "Late Lessons from Early Warnings: The Precautionary Principle 1896–2000". This paper summarises some of the definitional and other issues that arise from the report and subsequent debates, such as the contingent nature of knowledge; the definitions of precaution, prevention, risk, uncertainty, and ignorance; the use of different strengths of evidence for different purposes; the nature and main direction of the methodological and cultural biases within the environmental health sciences; the need for transparency in evaluating risks; and public participation in risk analysis. These issues are relevant to the risk assessment of electro-magnetic fields (EMF). Some implications of these issues and of the "late lessons" for the evaluation and reduction of risks from EMF are indicated.
© 2009 Published by Elsevier Ireland Ltd.

Keywords: Late lessons; EMF; Precautionary principle, Evaluating evidence

1. Introduction

The histories of fourteen well-known hazards and their harm, which include some chemicals: tributyl tin (TBT), benzene, polychlorinated biphenyls (PCBs), chlorinatedfluorocarbons (CFCs), methyl tert butyl ether (MTBE), sulphur dioxide, (SO_2) and Great Lakes pollution; two pharmaceuticals (diethylstilboestrol (DES) and beef hormones); two physical agents (asbestos and medical X-rays); one pathogen (BSE); and fisheries, have been reviewed by the European Environment Agency [1]. The purpose of the review was to see how societies had used, or not, the available scientific information in order to avoid or reduce hazards and risks, and at what overall cost.

Twelve "Late Lessons" were drawn which attempted to synthesise the very different experiences from the case studies into generic knowledge that can help inform decision making on potential hazards from, for example, GMOs [2,3], nanotechnologies [4], mobile phones [5,6] and such endocrine disrupting substances as phthalates, atrazine and bisphenol A [7–9]. These emerging issues are all cases for which the luxuries of hindsight are not yet available but where there is some plausible evidence of harm, and where exposures are widespread and generally rising.

The purpose of the twelve late lessons is to help societies to make the most of both past experience and current knowledge in order to anticipate and reduce the impact of future "surprises" from technologies, without stifling innovation.

The "late lessons" are reproduced in Box 1 .

2. The early use of precaution

John Graham, who was senior science policy advisor to President Bush, is a critic of the precautionary principle, but has nevertheless noted that:

Precaution, whether or not described as a formal principle, has served mankind well in the past and the history of public health instructs us to keep the spirit of precaution alive and well [10].

* Tel.: +45 33 36 71 42; fax: +45 33 36 71 28.
E-mail address: David.Gee@eea.eu.int.

0928-4680/$ – see front matter © 2009 Published by Elsevier Ireland Ltd.
doi:10.1016/j.pathophys.2009.01.004

Box 1: "The EEA Twelve Late Lessons"

A. "Identify/Clarify the Framing and Assumptions"

1. Manage "uncertainty" and "ignorance" as well as "risk".
2. Identify and reduce "blind spots" in the sciences used.
3. Assess and account for all pros and cons of action/inaction.
4. Analyse and evaluate alternative options to the agent/activity under scrutiny.
5. Take account of stakeholder values.
6. Avoid "paralysis by analysis" by acting to reduce hazards via the precautionary principle.

B. "Broaden Assessment Information"

7. Identify and reduce interdisciplinary obstacles to learning.
8. Identify and reduce institutional obstacles to learning.
9. Use "lay" and local as well as specialist knowledge.
10. Identify and anticipate "real world" conditions.
11. Ensure regulatory and informational independence.
12. Use more long-term (i.e. decades) monitoring and research.

Graham might have been thinking of the cholera episode of 1854 in Soho, when precaution did indeed serve the people of London well. Dr. John Snow, a well known but controversial London physician, was called in to investigate the cholera outbreak. He used the spirit of precaution to advise banning access to the polluted water of the Broad St. pump, which he suspected was the cause of a serious cholera outbreak. He based his recommendation partly on the evidence he had gathered from his comparative study of two South London populations, who were separately served by piped or well water; and partly on his innovative spatial epidemiological study of the Soho area which pointed to the Broad St. well as the source of water polluted by faeces. He considered this overall evidence was sufficiently strong to justify advising the precautionary action of removing the water pump handle, so that consumers would be forced to use less convenient but cleaner water supplies. His view was accepted by the local church authorities who administered the area.

We know now that Snow's conclusion was accurate. However, his views on cholera causation were not shared by the medical establishment of the day, the Royal College of Physicians and the London Board of Health, who had considered Snow's thesis and rejected it as 'untenable' and biologically implausible [1]. They believed that cholera was caused by airborne, not water borne, pollution. Their scientific "certainty" was increasingly challenged by Snow and others until Koch in Germany finally isolated the cholera vibrio in 1883, thus removing the last remaining doubt about the veracity of Snow's water pollution hypothesis.

The Snow story illustrates many of the key elements of the PP issue that are relevant to today's health and environment controversies, viz conflicting expert advice; competing scientific paradigms; the strength of scientific evidence needed to justify action; the long time lag between *observing* compelling associations and *understanding* their mechanisms of action; and the pros and cons of being wrong in taking action to remove risks, compared to the pros and cons of inaction.

The histories of TBT, PCBs and the other cases in the EEA "Late Lessons" report provide further illustrations of these points.

3. On paradigms and mechanisms of action

Scientists can cling to their favourite paradigm for decades—as with supporters of the air pollution theory in the cholera example between 1854 and 1883, despite mounting evidence that they are likely to be wrong. This passion for the prevailing paradigm is not uncommon. Max Planck, the Nobel physicist noted darkly that old paradigms only really die out when their promoting professors also die: "A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it" [11].

In similar vein, the IPPC has cautioned the scientific authors of its climate change assessment reports against:

a tendency for a group to converge on an expressed view and become over confident in it. Views and estimates can also become anchored on previous versions or values to a greater extent than is justified [12].

This "power of the prevailing paradigm" is relevant to the current controversy over mobile phones, where the dominant view of WHO, the EU, and many others is that EMF-RF (radio frequency) energy has to be sufficiently large to cause the heating of biological tissue if it is to cause significant harm [13–15]. The current ICNIRP guidelines for limiting unacceptable RF exposures are derived from this paradigm and are therefore:

based on short term, immediate health effects, such as stimulation of peripheral nerves . . . and elevated tissue temperatures [13].

This majority view is opposed by those who think that much lower levels of EMF have the potential to cause harm via their capacity to disturb cell signalling or stress response systems that use very small changes in electro-magnetic fields [16–19].

Is the EMF field witnessing one of those shifts in prevailing paradigms that Thomas Kuhn noted had characterised progress in many fields of science? [20]

It can be difficult to accept that something is happening if you do not understand how it can be happening. A major reason why some scientists hang on to their preferred paradigm when evidence against it is mounting is that they need not only to observe a strong association between a cause and an effect but also to understand the mechanisms of biological action that link them. However, this can take decades. From the *association* between exposure to water polluted with human faeces and cholera, observed by Snow in 1854, to Koch's discovery of the *mechanism of action*, took 30 years of further scientific inquiry.

Such a long time lag between acknowledging compelling associations and understanding their mechanisms of action is a common feature of scientific inquiry, as illustrated by many of the case studies in the EEA report. Biological and ecological understanding about exactly how these exposures caused harm is still absent, decades after the associations were accepted as sufficient to justify preventive actions.

With EMF, there is currently no *established* knowledge about the mechanisms of biological action that could explain the consistent associations between EMF-ELF (extremely low frequency) exposure from overhead electrical power lines and childhood leukaemia. However, there is some evidence of *plausible* biological mechanisms. These include hypotheses concerning "information physics" [21]; melatonin [22]; oxidative stress [19]; indirect effects via cancer promotion; and the radical pair mechanism, which according to the Swedish Radiation Protection Authority, is "*probably the most plausible hypothesised mechanism*" [23]. Some or all of the above mechanisms, possibly in combination with other stressors and genetic configurations, is likely to eventually provide mechanistic explanations for the observed biological effects of EMF-ELF.

Despite this lack of mechanistic knowledge, and a general lack of corroborating animal evidence, the International Agency for Research on Cancer (IARC-WHO) recognised ELF from such magnetic fields as possibly carcinogenic in 2002, based on more than 30 positive epidemiological studies which had been completed since the first "early warning" observation in 1979 [24]. Other scientists do not believe the association between ELF and childhood leukaemias, given the paucity of mechanistic knowledge. However, recent animal and human evidence seems to be filling some of this knowledge gap [25].

The ELF story has parallels with that concerning the ionising X-rays which were routinely given to pregnant women before the early warning of Alice Stewart in the 1950s. She had observed a twofold excess of childhood leukaemias in women given X-rays during pregnancy. Her findings were eventually accepted by the 1970s, despite the continuing absence of knowledge about mechanisms of action: and such routine X-ray exposures were then stopped [26].

The current situation with the EMF-RF exposures from mobile phones is characterised by some positive yet generally inconsistent epidemiological evidence [27–29], by a general absence of animal evidence; and by little established knowledge of possible mechanisms of carcinogenic action.

The question therefore arises: should actions that seem likely to protect the health of the public have to wait for knowledge about mechanisms of action? The precautionary principle was designed to justify actions to protect the public and the environment in the absence of some significant knowledge, and could be used to justify exposure reductions to EMF, despite current gaps in knowledge.

Could the unfolding story of EMF be a repetition of these earlier histories of ionising radiation exposures where evidence of harm was only "established" some twenty or more years after the first early warning?

4. Early warnings

When dealing with newly emerging hazards it can be helpful to use historical examples to illustrate what a scientifically based early warning looks like. It is often difficult to properly recognise such warnings when they occur.

A good example is that provided by the UK Medical Research Council's Swann Committee in 1969. The Committee was asked to assess the evidence for risks of resistance to antibiotics in humans, following the prolonged ingestion of trace amounts of antibiotics arising from their use as growth promoters in animal feed [30]. They concluded that:

Despite the gaps in our knowledge ... we believe ... on the basis of evidence presented to us, that this assessment is a sufficiently sound basis for action ... The cry for more research should not be allowed to hold up our recommendations'. ... 'sales/use of AFA should be strictly controlled via tight criteria, despite not knowing mechanisms of action, nor foreseeing all effects [31].

Despite the gaps in knowledge, the need for much more research, and considerable ignorance about the mechanisms of action, the available evidence was acknowledged by the Swann Committee as sufficient to justify the need for the authorities to restrict the possibility of public dietary exposures to antibiotics from animal growth promoters.

This early warning was initially heeded, but was then progressively ignored by the pharmaceutical companies and regulatory authorities, which wanted more scientific justification for restricting profitable anti-microbial growth promoters. However, the use of antibiotics as growth promoters was finally banned in the EU in 1999, following the lead of Sweden in 1985 [30].

Pfizer, the main supplier of such antibiotics in Europe, appealed against the European Commission decision to ban their product, pleading, inter alia, an insufficiency of scientific evidence. They lost the case at the European Court of Justice [32]. This case further clarified the appropriate use and

application of the precautionary principle in circumstances of scientific uncertainty and of widespread, if low, public exposures to a potentially very serious threat.

On EMF there has been a number of early warnings about potential risks at low levels of exposure, culminating in the Bioinitive report of 2007 [33]. This prompted the EEA to also issue an "early warning":

Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives [34].

It is possible that such early warnings, particularly on RF from mobile phones, issued by the EEA and others, will turn out to be incorrect. This will only be established with time, and the hindsight it brings. However, the EEA would rather be wrong in raising concerns that turn out not to be justified, than being wrong in not issuing an early warning if the potentially serious hazards from RF technology turn out to be real. Large numbers of people are potentially exposed to RF, particularly children who are generally more susceptible to the potential harm. Reducing RF exposures in response to a mistaken early warning is preferable to not reducing exposures to a hazard that turns out to be real, and largely irreversible. Moreover, encouraging such reduction could help to stimulate technical innovation.

5. The importance of timing

The issue of time is a critical issue for risk analysis and application of the precautionary principle.

For example, the time from the first scientifically based early warnings (1896 for medical X-rays, 1897 for benzene, 1898 for asbestos), to the time of policy action that effectively reduced damage, was often 30–100 years, during which exposure increased considerably (Table 1).

One consequence of such failures to act in good time (e.g. on CFCs or asbestos) is greater and irreversible damage over longer time periods. For example, extra natural radiation coming through the ozone hole will cause many tens of thousands of extra skin cancers in today's children but the cancers will only peak around the middle of this century because of the long latent period between exposure and effect. Over a decade's worth of extra skin cancers could have been avoided if action had been taken on the first early warning, (which was subsequently deemed robust enough to justify giving the Nobel prize for Chemistry to its authors), rather than on the discovery of the ozone hole itself. Other negative impacts from the damaged ozone hole include eye cataracts and reduced crop productivity.

Such long-term but foreseeable impacts raise liability and compensation issues, including appropriate discount rates (if any) on future costs and benefits. These issues, which involve value and equity choices, need also to be discussed by stake-

Table 1

Late Lessons chapter	Date of first Early Warning	Date of Effective risk reduction action	Years of substantial inaction
Fisheries: taking Stock	1376	1995–2008 "responsible" management: which is not very effective	Hundreds...
Radiation: Early Warnings, Late Effects	1896	1961–1996 UK etc., then EU laws	65
Benzene: occupational setting	1897	1978 Benzene voluntarily withdrawn from most consumer products, US	81
Asbestos: from "magic" to malevolent material	1898	1999 EU ban by 2005	101
PCBs and the Precautionary Principle	1899	1970–80s:EU and US restrictions; phase out by 2010	c. 100
Halocarbons, the ozone layer and the Precautionary Principle	1974	1887–2910 global ban on CFCs + other Ozone depleters	10–30
DES: long-term consequences of pre-natal exposure	1938	1971–1985 US, EU, global ban	30–50
Antimicrobials as growth promoters: resistance to common sense	1969	1999 EU ban	30
SO_2: from protection of human lungs to remote lake restoration	1952 (lung) 1968 (lakes)	1979–2001 increasing EU etc restrictions leading to c 90% reduction on 1975 levels by 2010	25–55
MTBE in petrol as a substitute for lead	1960 taste/odour/persistence in water	2000 undesireable in Denmark/California: permitted elsewhere	40+
Great Lakes contamination	1962/3	1970s DDT banned in N America& EU. 2000 debates continue about persistent health damaging pollution	10–?
TBT antifoulants: a tale of ships, snails and imposex	1976–81 French oysters collapse	1982–7 French, UK then NE Atlantic ban; 2008 global ban	5–30
Beef Hormones as growth promotors	1972/3 oestrogen effects on wildlife	1988 EU ban, US continues	16+
Mad cow disease-reassurances undermined precaution	1979–1986	1989 Partial; 1996 total ban	10–17

holder groups. Experience in the climate change field with these long-term issues [35] may be helpful for the EMF issue.

Timing is also a critical issue for the assessment of risks. Many agents seem to be most damaging during sensitive windows of biological opportunity, either at the foetal stage of development [36], or when the host is susceptible because of an immune response deficiency, or of impacts from other stressors.

Timing is relevant to several biological end points as indicated in a review of the evidence on endocrine disrupting substances:

the time of life when exposures take place may be critical in defining dose–response relationships of Endocrine disrupting substances for breast cancer as well as for other health effects [37].

Responding to these issues of timing involves using lower strengths of evidence to justify action at earlier times in the exposure history of the stressors that inflict damage during specific windows of vulnerability, such as during foetal or early childhood development [38]. The wide exposure of children to EMF brings the timing of actions to reduce exposures into critical focus.

6. Knowledge and ignorance, prevention and precaution

The Broad St. pump example, and the other case studies in the EEA report serve to illustrate the contingent nature of scientific knowledge. Today's scientific certainties can be tomorrow's mistakes, and today's research can both reduce and increase scientific uncertainties, as the boundaries of the "known" and the unknown expand (Fig. 1).

It is common to hear the call for "more research" to remove uncertainties before any actions are taken to reduce hazards. However, such further research may not only take many years but tomorrow's knowledge, in addition to removing some uncertainties, is likely to identify previously unknown

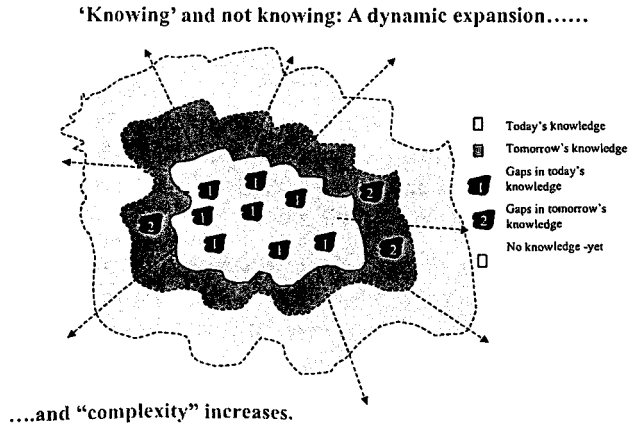


Fig. 1. Knowing and not knowing both espand.

sources of both uncertainty and ignorance. These new uncertainties can then be used as reasons for continued inaction on hazard reduction: "paralysis by analysis".

Socrates observed some time ago:

I am the wisest man alive, for I know one thing, and that is that I know nothing [39].

Such an approach to knowledge encourages humility in scientists rather than the hubris demonstrated by those scientists who, for too many years, professed certainties about the absence of harm from X-rays, asbestos, CFCs etc. These "certainties" turned out to be misplaced as knowledge expanded [1].

Many great scientists since Socrates have also displayed much humility in the face of acknowledged ignorance. Isaac Newton provided an elegant illustration of this towards the end of his life of discoveries:

to myself I seem to have been only like a boy playing on the seashore, and diverting myself now and then, finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me [40].

This was an early lesson in humility that seems to have been lately forgotten by many of the scientists and politicians who deal with hazards to the public and environment.

The distinction between uncertainty and ignorance also has significant implications for risk analysis and management [41]. Uncertainties arise, inter alia, from the known gaps in knowledge, from imprecise exposure sampling and monitoring; and from the assumptions and simplifications of models used to describe complex reality. Scientists involved in regulatory risk assessments try to take account of some of these uncertainties by using arbitrary safety factors to arrive at "acceptable" exposure limits.

Acknowledging ignorance, however, involves acknowledging the unknown unknowns, as well as the sometimes unknowable unknowns that arise from complex and unpredictable biological and ecological systems and the random variations that are common to them [42,43]. It is obviously not possible to just use safety factors applied to "known" associations to account for such lack of knowledge.

States of ignorance are also the source of new scientific discoveries as well as of unpleasant "surprises" such as the mesothelioma cancer from asbestos, the hole in the ozone layer, or the reversed sexuality in the sea snails contaminated by the TBT biocide in marine anti-fouling paints [44].

Foreseeing and preventing hazards in the context of ignorance presents particular challenges to decision-makers. Ignorance ensures that there will always be surprises, and at first sight it looks impossible to do anything to avoid, or mitigate, them. However, there are some measures that could help minimise the consequences of ignorance and the impacts of surprises:

- using the intrinsic properties of potential stressors as generic predictors for unknown but possible impacts e.g.

the persistence, bioaccumulation and spatial range potential of chemical substances [45];

- reducing specific exposures to potentially harmful agents on the basis of credible 'early warnings' of initial harmful impacts, thus limiting the size of any other 'surprise' impacts from the same agent, such as the asbestos cancers that followed asbestosis; and the PCB neurotoxicological effects that followed its wildlife impacts;
- promoting a diversity of robust and adaptable technological and social options to meet human needs, which then limits technological 'monopolies' (such as those of asbestos, CFCs, PCBs etc.), and therefore reduces the scale of any 'surprise' from any one technological option;
- accepting significant biological and ecological effects, such as inflammatory responses, or changing sex ratios, as sufficient evidence of potentially adverse effects to justify hazard reduction, without waiting for the adverse effects themselves to arrive;
- using more long-term research and monitoring of what appear to be "surprise sensitive sentinels", such as frogs, bees and foetuses, in order to identify "early warnings" earlier;
- using scenarios and stakeholder involvement to help foresee and anticipate implications of particular technological and social pathways.

Some of these approaches are relevant to EMF.

The distinction between *prevention* and *precaution* is also important. Preventing hazards from "known" risks is relatively easy and does not require precaution. Banning smoking, or asbestos, today requires only acts of *prevention* to avoid the well-known risks. However, it would have needed *precaution* (or foresight, based on a lower strength of evidence), to have justified exposure reductions to the then uncertain hazards of asbestos exposure in the 1930s–50s, or of tobacco smoke in the 1950s–60s.

Such precautionary acts then, if implemented successfully, would have saved many thousands of lives and, in the case of asbestos, stimulated innovation in the insulation and other asbestos using industries decades earlier than has been the case.

Similarly, it would need precaution to justify reducing exposures to an IARC category two carcinogen, such as EMF, but only prevention to avoid the cancer risk from a class one carcinogen, such as ionising radiations, where the evidence for action is very well established.

There has been much debate generated by the different meanings attached to these and other terms commonly used in debates on hazards, such as "prevention", "precaution", "risk", "uncertainty" and "ignorance". Table 2 attempts to clarify these definitions, using some of the "Late Lessons" case studies as illustrations.

There is also frequent confusion between the *strength of evidence* needed to justify any action to reduce risks, and the *type of action* deemed to be appropriate: the two are not directly connected. For example, there is very strong evidence that cars harm people, but they are not banned from most places. In contrast, slight evidence of possible birth defects arising from taking a pregnancy pill would usually be sufficient to justify banning that pill.

7. The precautionary principle: some definitions and interpretations

The Vorsorgeprinzip, (the "precautionary", or "foresight") principle, only emerged as a specific policy tool during the German debates on the possible role of air pollution as a cause of "forest death" in the 1970–80s.

An increasing awareness of ecological complexity and uncertainty during the 1980–90s led to debates on the Vorsorgeprinzip shifting from Germany to the international level, initially in the field of nature conservation [46] but then particularly in marine pollution, where an overload of data accompanied an insufficiency of knowledge [47]. This absence of knowledge generated the need to act with precaution to reduce the large amounts of chemical pollution entering the North Sea.

Since then over 60 international treaties, including the Third North Sea Ministerial Conference, 1990, have included reference to the precautionary principle, or, as the Bush negotiators prefer to say, the precautionary approach. (A recent legal review points out that there is little, if any practical difference between these two concepts [48].)

The Treaty of the European Union cites the precautionary principle thus:

Community policy on the environment ... shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should, as a priority, be rectified at the source, and the polluter should pay [49].

Although only cited in the environment part of the EU Treaty, the precautionary, prevention and polluter pays principles also apply to health and consumer affairs, as European Court of Justice decisions have made clear [50].

Unfortunately, these principles, as well as the important and legally required *proportionality principle*, which limits disproportion between the costs and benefits of precaution or prevention, are not defined in the EU Treaty. However, their usage has been clarified in over 100 court cases [48].

A definition of the precautionary principle that is often cited by supporters and detractors alike is that from the The North Sea Declaration, which calls for:

action to avoid potentially damaging impacts of substances, even where there is no scientific evidence to prove a causal link between emissions and effects (my emphasis).

Critics of the precautionary principle claim that this definition appears to justify action even when there is "*no scientific evidence*" that associates exposures with effects. However, the N. Sea Conference text clearly links the words "no scien-

Table 2
Towards a clarification of key terms.

Situation	State and dates of knowledge	Justification for action
• Risk	Known' impacts; 'known' probabilities e.g. asbestos 1999	*Prevention*: action taken to reduce known hazards e.g. eliminate exposure to asbestos dust
• Uncertainty	'Known' impacts; 'unknown' probabilities e.g. antibiotics in animal feed and associated human resistance to those antibiotics 1999	*Precautionary Prevention*: action taken to reduce exposure to plausible hazards e.g. ban antibiotic growth promotors
• Ignorance	'Unknown' impacts and therefore 'unknown' probabilities e.g. the 'surprise' ozone hole from (CFCs), pre-1974	*Precaution*: action taken to anticipate, identify and reduce the impact of 'surprises'

Source: Amended from the "Late Lessons" report, EEA 2001.

tific evidence" with the words "to prove a causal link" (my emphasis).

We have already seen with the Broad St. pump example that there is a significant difference between the evidence needed to show an "*association*" between a pollutant and its harm, and evidence which is robust enough to "prove" a *causal* link, which requires a very much higher strength of evidence. Bradford Hill pointed this out in his classic paper on association and causation in public health which he wrote at the height of the smoking controversy [51].

The N. Sea Declaration says that the absence of the strong evidence needed to support causality is not a valid reason for inaction where there is widespread and potentially hazardous exposures and some plausible evidence of potential harm.

Despite increasing use of the precaution principle there is still much disagreement and discussion about its practical application. This is particularly due to the absence of an EU definition in regulatory texts, and to disputes over the sufficiency of scientific evidence needed to justify public policy action.

For example, many "definitions" of the precautionary principle or approach in the 60 or so Treaties and Conventions that now include this concept use a triple negative: that is, they identify the *absence* of strong scientific evidence (e.g. of "full" certainty") as a reason that *cannot* be used to justify *not* acting, And they do not specify what a sufficiency of evidence would be that could justify taking action.

Some other widely cited definitions of the precautionary principle, notably the Wingspread and UNESCO definitions, are rather long, and include items that are not strictly part of a definition, such as the *process* by which decisions are taken (i.e. participatory, or not); and the allocation of the *burden of proof* to risk makers or risk takers: the latter is a separate issue that societies have dealt with without recourse to the precautionary principle.

For example, European and other societies have long placed the pre-market burden of establishing reasonable grounds for the safety of medicines, pesticides, nuclear plants and large construction projects on those who wish to provide such products or projects, Other potentially harmful agents, such as the 100,000 or so existing chemicals in consumer products, have been placed on the market without such pre-market burdens. Although pre-market testing or assessment is more precautionary than post market surveillance, it does not require justification from the precautionary principle.

There have been further definitions and clarifications of the precautionary principle from, for example from the EU Council of Ministers; in EU case law; and in the regulation establishing the new European Food Safety Authority, EFSA [52].

The judgement of the European Court of Justice in the BSE case illustrated a general definition which many authoritative commentators consider contains most of the necessary elements of the precautionary principle:

Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent [53].

The WHO Declaration from the Fourth Ministerial Conference on Environment and Health [54] also refers to the precautionary principle. An explanatory background paper recommends that the principle:

should be applied where the possibility of serious or irreversible damage to health or the environment has been identified and where scientific evaluation, based on available data, proves inconclusive for assessing the existence of risk and its level but is deemed to be sufficient to warrant passing from inactivity to policy alternatives [55].

A recent report from the Health Council of the Netherlands on the precautionary principle provides a clear and cogent summary of the issues raised by its use [56].

However, there remains an absence of a clear definition at EU level so the European Environment Agency (EEA), in response to the debates on the precautionary principle since its 2001 report, has produced a working definition of the precautionary principle.

The Precautionary Principle provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment, using an appropriate level of scientific evidence, and taking into account the pros and cons of action and inaction [8].

The definition is proving useful in promoting a shared understanding of the precautionary principle. It is explicit in specifying both uncertainty and ignorance as contexts for applying the principle; it is couched in the affirmative rather

than the negative; and it explicitly acknowledges that a case specific sufficiency of scientific evidence is needed to justify public policy actions, given the pros and cons of action or inaction.

The definition also explicitly widens the conventionally narrow, and usually quantifiable, interpretation of costs and benefits to embrace the wider and sometimes unquantifiable, "pros and cons". Some of these wider issues, such as loss of public trust in science, are unquantifiable, but they can sometimes be more damaging to society than the quantifiable impacts: they therefore need to be included in any comprehensive risk assessment.

But what is "an appropriate strength of evidence" that would justify taking action under the precautionary principle to reduce exposures and risks?

8. Establishing evidence for action

All serious applications of the precautionary principle require some plausible evidence of an association between exposures and current, or potential, impacts.

For example, the Communication from the EU on the precautionary principle [57] specifies that "reasonable grounds for concern" are needed to justify action, but it does not say that these grounds will vary with the specifics of each case: nor does it explicitly distinguish between risk, uncertainty and ignorance.

The strength of scientific evidence that would be appropriate to justify public action clearly must vary with the pros and cons of being wrong with action or inaction in the specific circumstances of each case. These circumstances include the nature and distribution of potential harm; the justification for, and the benefits of the agent or activity under suspicion; the availability of feasible alternatives; and the overall goals of public policy. Such policy goals can include the achievement of the "high levels of protection" of public health, of consumer safety, and of the environment, required by the EU Treaty.

The use of different strengths of evidence for different purposes is not a new idea.

For example, a high strength of evidence such as "beyond all reasonable doubt" is used to achieve good science where A is generally accepted as causing B only when the evidence is very strong. Such a high level of proof is also used to minimise the costs of being wrong in the criminal trial of a suspected murderer, where it is usually regarded as better to let several guilty men go free, when reasonable doubt about their guilt cannot be eliminated, than it is to wrongly convict an innocent man.

However, in a different trial setting, where a citizen seeks compensation for harm that is possibly due to negligent treatment at work, the courts in many European and other societies will use a lower strength of evidence, commensurate with the costs of being wrong in this different situation. An already injured party is given the benefit of the doubt by the use of a medium level of proof, such as "balance of evidence, or probability". This is justified on the grounds that it is more acceptable to give compensation to someone who was *not* treated negligently than it is to *not* provide compensation to someone who was treated negligently. The "broad shoulders" of insurance companies are seen as able to bear the costs of mistaken judgements rather better than the much narrower shoulders of an injured citizen.

In each of these two illustrations it is the nature and distribution of the costs of being wrong that determines the strength of evidence that is "appropriate" to the particular case, based essentially on ethical grounds. The choice of an appropriate strength of evidence in each case is therefore a societal not a scientific issue.

This has long been recognised. Bradford Hill, cited above, drew attention to the social responsibility of scientists whose work involves public health. He concluded his classic 1965 paper on association and causation in environmental health with a "call for action" in which he also proposed case specific and differential strengths of evidence.

His three illustrative examples ranged from "relatively slight" to "very strong" evidence, depending on the nature of the potential impacts and of the pros and cons of being wrong. These varied between a possibly teratogenic medicine for pregnant women; a probable carcinogen in the workplace; and government restrictions on public smoking or diets [51].

In the field of cancer, the International Agency for Research on Cancer also uses several types of scientific evidence to categorise their strengths of evidence on carcinogens [58].

Identifying an appropriate strength of evidence has also been an important issue in the climate change debates. The International Panel on Climate Change (IPCC) discussed this issue at length before formulating their 1995 conclusion that "on the balance of evidence" mankind is disturbing the global climate. They further elaborated on this issue in their 2001 report where they identified seven strengths of evidence that can be used to characterise the scientific evidence for a particular climate change hypothesis. By 2007 the evidence for human induced climate change had strengthened to a "reasonable certainty" [59].

Table 3 provides the middle 5 of these strengths of evidence from the IPPC and illustrates their practical application to a variety of different societal purposes.

In the risk assessments of EMF published so far there has been little explicit discussion about the choice of the strength of evidence used in the assessments. The vague term "no established evidence" is often used to characterise the absence of some strength of evidence that would convince the particular scientists doing the risk assessment that a hazard existed. There is little if any discussion about for whom the evidence is said to be not established (risk takers or risk makers), nor about for what purpose (warning labels, or low cost exposure reductions, for example.).

Table 3
Different levels of proof for different purposes.

Different levels of proof for different purposes: some examples and illustrations			
Probability	Quantitative descriptor (Probability bands based on IPCC 2001)	Qualitative descriptor	Illustrations
100% probability	Very likely 90–99%	• "Statistical significance"	• Part of strong scientific evidence for "causation"
		• "Beyond all reasonable doubt"	• Most criminal law. And the Swedish Chemical law, 1973, for evidence of "safety" of substances under suspicion-burden of p roof on manufacturers
	Likely (66–90%)	• "Reasonable certainty"	• Food Quality Protection Act, 1996 (US)
		• "Sufficient scientific evidence"	• To justify a trade restriction designed to protect human, animal or plant health under World Trade Organisation Sanitary and Phytosanitary (SPS) Agreement, Art. 2.2, 1995
	Medium Likelihood (33–66%)	• "Balance of evidence"	• Intergovernmental Panel on Climate Change 1995 & 2001
		• "Balance of probabilities"	• Much Civil and some administrative law
		• "Reasonable grounds for concern"	• European Commission Communication on the Precautionary Principle 2000
		• "Strong possibility"	• British Nuclear Fuels occupational radiation compensation scheme, 1984 (20–50% probabilities triggering different awards up to 50% + , which then triggers full compensation)
	Low Likelihood (10–33%)	• "Scientific suspicion of risk"	• Swedish Chemical law, 1973, for sufficient evidence to take precautionary action on potential harm from substances-burden of proof on regulators
		• "Available pertinent in formation"	• To justify a provisional trade restriction under WTO SPS Agreement, Art. 5.7 where "scientific information is insuffiicient"
	Very Unlikely (1–10%)	• Low risk	• Household fire insurance
		• "Negligible and in significant"	• Food Quality Protection Act, 1996 (US)

Source: EEA (2002).

An exception is the Californian EMF-ELF risk assessment which was much more transparent and explicit about these critical issues [60].

Establishing a sufficiency of evidence for whom, and for what purpose, involves value judgements: such issues therefore require public participation.

9. Public participation in risk analysis

Choosing an appropriate strength of evidence for a particular case is not a scientific issue but a social choice. It is therefore necessary to involve the public in decisions about serious hazards and their avoidance: and to do so for all stages of the risk analysis process, as recommended by several authorative bodies during the last 10 years [61,62,63,64,56,65]. Three of the "twelve late lessons" of the EEA report (numbers 5, 9 and 10 in Box 1) also encourage the involvement of stakeholders at all stages of risk analysis.

Fig. 2 based on the above reports, illustrates the iterative nature of risk assessment, risk management, and risk communication; the links between them; and the involvement of stakeholders at every stage, albeit with different intensities.

The existing International and European arrangements for risk analysis, and for the setting of public exposure limits for EMF and other issues such as food [66], do not seem to reflect these recommendations for opening up the process of risk analysis, including risk assessment, to stakeholder participation. Instead they largely retain the older, linear approach where risk assessment is separated from risk management and communication and where communication is largely one way, i.e., from scientists to managers to the public.

The best available science is therefore a necessary but not a sufficient condition for sound public policy making on potential threats to health and the environment, such as from EMF. Where there is scientific uncertainty and ignorance "it is primarily the task of the risk managers to provide risk assessors with guidance on the science policy to apply in their risk assessments" [67]. The content of this science policy advice, as well as the nature and scope of the questions to be addressed by the risk assessors, need to be formulated by the

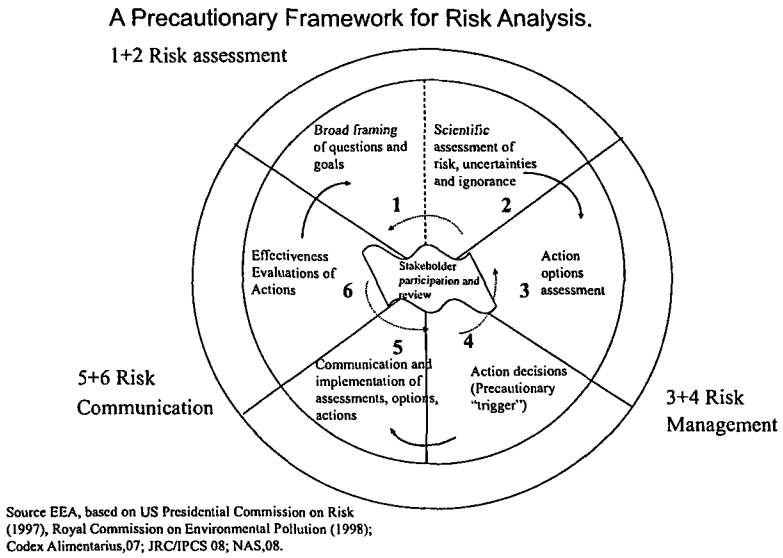


Fig. 2. A Precautionary risk analysis framework.

risk managers and relevant stakeholders at the initial stages of the risk analysis, as indicated in Fig. 2.

It is not easy to involve the public in all stages of risk analysis and in helping to set associated research agendas and technological trajectories [68,69]. However, there are some useful experiences, in both Europe and the USA, with focus groups, deliberative polling, citizens juries, and extended peer review, which are exploring appropriate ways forward [70,71].

The SAGE stakeholder process in the UK, which focused on ELF from power lines, provides a useful illustration of stakeholder engagement [72].

Public participation is particularly essential when future technological and social pathways, and associated hazards, are unpredictable: being wrong together is more socially robust than letting experts alone make the mistakes.

But why are there enough "mistakes", from delayed policy actions to prevent serious harm, to fill several volumes of Late Lessons reports?

10. False positives and false negatives

The fourteen case studies in the Late Lessons Report are all examples of "false negatives" in the sense that the agents or activities were regarded as not harmful for many years before evidence showed that they were harmful. Attempts were made to include a "false positive" case study in the report (i.e. where actions to reduce potential hazards turned out to be unnecessary), but neither authors nor sufficiently robust examples were found.

Providing evidence of "false positives" is more difficult than with "false negatives" [73]. For example, how robust, and over what periods of time, does the evidence on the absence of harm have to be before concluding, with confidence, that a restricted substance or activity is without significant risk?

Volumes 2 of "Late Lessons", which the EEA will publish in 2009, will explore the issues raised by false positives, including lessons to be learned from such apparent false positives as the EU ban on food irradiation and the hazardous labelling of saccharin in the US [74].

But why are there so many "false negatives" that have been so damaging to health or environment? And how might this be relevant to EMF?

The first Late Lessons volume of case studies provided two main answers: the bias within the health and environmental sciences towards avoiding "false positives", which thereby generates more "false negatives": and the dominance within societal decision-making of short term, specific, economic and political interests over the longer term, diffuse, and overall welfare interests of society. The latter point needs to be further explored, particularly by the political sciences: the current and increasing dominance of the short term in markets and in parliamentary democracies makes this an urgent issue.

Since the publication of "Late Lessons" the EEA has further explored the second cause of "false negatives" i.e. the issue of bias within the health and environmental sciences. Table 4 lists eighteen common features of methods and culture in the environmental and health sciences and shows their main directions of error. Most tend towards generating "false negatives".

Table 3 is derived from papers presented to a conference on the precautionary principle organised by the Collegium Ramazzini, the EEA, the WHO and NIEHS in 2002 [75]. It tries to communicate the main directions of the biases within the environmental and health sciences which decision makers and the public should be aware of as they debate the evidence on emerging hazards such as EMF.

Table 4
ON BEING WRONG: Environmental and health sciences and their main directions of error.

Scientific studies	Some methodological features	Main[a] directions of error-increases chances of detecting a:
Experimental	• High doses	• False *positive* (negative for low dose effects)
Studies	• Short (in biological terms) range of doses	• False negative
(Animal Laboratory)	• Low genetic variability	• False negative
	• Few exposures to mixtures	• False negative
	• Few Foetal-lifetime exposures	• False negative
	• High fertility strains	• False negative (developmental/reproductive endpoints)
Observational	• Confounders	• *False positive* (negative with multi-causality?)
	• Recall bias	• *False positive*
Studies	Inappropriate controls	• *False positive*/negative
(Wildlife & Humans)	• Non-differential exposure misclassification	• False negative
	• Inadequate follow-up	• False negative
	• Lost cases	• False negative
	• Simple models that do not reflect complexity	• False negative
Both	• Publication bias towards positives	• *False positive*
Experimental and observational studies	• Scientific cultural pressure to avoid false positives	• False negative
	• Low statistical power (e.g. From small studies)	• False negative
	• Use of 5% probability level to minimise chances of false positives	• False negative
	• Much scrutiny of positive studies cf. negative studies	• False negative

[a] Some features can go either way (e.g. inappropriate controls) but most of the features mainly err in the direction shown in the table.

11. Towards realism about complex reality

Max Planck observed that "reality is ... just a very thin slice of that vast range of what our thoughts try to encompass" [76]. EMF scientists and risk assessors need not only to take account of the false negative/positive biases described above but they should also take more account of "that vast range" of other realities which characterise the EMF issue. These include multi-causality; thresholds; timing of dose; sensitive sub-populations; sex, age, genetics, and immune status of the host; cumulative exposures to EMF and other stressors; information physics; effects below the thresholds of such "acute" impact as tissue heating; non-linear dose–response relationships; "low dose" effects; the absence of unexposed controls; and the effects arising from disturbing the balance between opposing elements in complex biological systems, i.e. the "harmony of opposites" which Heraclitus noted many centuries ago.

In the EMF debate these complexities are often subsumed under many simplifying assumptions. For example, the WHO review of power line ELF states that:

Based on known physical principles and a simplistic biological model, many authors have argued that average magnetic fields of 0.3–0.4 micro tesla are orders of magnitude below levels that could interact with cells or tissues and that such interactions are thus biophysically implausible [77].

In the context of expanding scientific knowledge, the "implausibility" of biological interactions may not be a robust basis on which to dismiss positive epidemiological or experimental observations, especially when the biological models being used are "simplistic".

The case studies in the EEA report illustrate the surprises that arise from real life ecological and biological complexities and which may carry some lessons for the EMF debate. For example, the unfolding of the TBT story was accompanied by an increased appreciation of scientific complexity. This arose from the discoveries that the known acute effects provided no indication of the chronic impacts that were caused by very low doses (i.e. in parts/trillion); that high exposure concentrations were found in unexpected places e.g. in the marine micro-layer; and that bioaccumulation in higher marine animals, including sea-food for human consumption, was much greater than expected. The early and prescient actions on TBT exposure reduction in France and the UK in 1982–85 were based only on a medium 'strength of evidence' for the 'association': evidence that was sufficient to infer 'causality', or to identify 'mechanisms of action' came much later.

We were lucky with TBT: a highly specific, initially uncommon impact (imposex) was quickly linked to one chemical, TBT. This is not likely to happen with the multi-causal and more common impacts such as neurodevelopmental diseases and dysfunctions, or cancers, which are the more complex impacts from EMF that are under suspicion.

Some key lessons from the DES story are also relevant to EMF exposures [78].

These include the realisation that the absence of visible and immediate teratogenic effects is not robust evidence for the absence of reproductive toxicity; and the timing of the dose clearly determined the poison, in contrast to the conventional dictum in toxicology, articulated by Paracelsus, that 'the dose determines the poison'.

DES is now a well-studied compound, with over 20,000 publications, yet many doubts persist about its mechanisms of action more than 30 years after it was banned on compekking observatory evidence that has since become more so. If we still have few biological certainties about DES after so much time and research, what should our attitude be towards relatively little understood hazards, such as other endocrine disrupting substances and EMF?

The scientists and risk assessors of EMF need not only to acknowledge the "surprises" that arise from complex realities but also the asymmetry of measurement precision between gene typing and environmental exposure assessment. As Vineis has observed, such asymmetry is likely to lead to an underestimation of the effects of environment and an overestimation of the effects of genes in the gene/environment interactions that are involved in most public health issues, including EMF [79].

The research implications arising from multi-causality, and from the systemic interactions between genes, host conditions and environmental stressors, seem not to have been fully recognised in the environmental and health sciences.

Sing has noted that:

neither genes nor their environments, but their interactions, are causations .... pretending that the aetiology of common diseases like CHD, cancer, diabetes and psychiatric disorders are caused by the independent actions of multiple agents is deterring progress [80].

He went on to call for:

"research that reflects the reality of the problem" and notes that "a reductionist approach that has no interest in complexity discourages imaginative solutions ... we need an academic environment that puts greater value on how the parts are put together".

Such a systems approach to multiple and cumulative stressors seems to be largely absent from much research and risk assessment of EMF. Recent progress in dealing with cumulative stressors in the chemical field may be of use to EMF scientists [81].

12. Towards transparency in evaluating "weight of evidence"

Since 1965 overall evaluations of scientific evidence for policy making on health hazards has often, implicitly or explicitly, been based on the nine, "Bradford Hill Criteria", which Bradford Hill actually called "features" of evidence [51]. These were produced in response to the smoking and health controversy of the 1960s.

One of the apparently more robust of the nine "criteria", consistency of research results, which is a much discussed issue in the current EMF debate, may not be so robust in the context of multi-causality, complexity and gene/host variability.

Prof. Needleman, who provided the first of what could be called the second generation of early warnings on lead in petrol in 1979, has subsequently observed that:

Consistency in nature does not require that all or even a majority of studies find the same effect. If all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious [82].

It follows that the *presence* of consistency of results between studies on the same hazard can provide some of the robust evidence needed to establish a causal link, but the *absence* of such consistency may not provide very robust evidence for the absence of a real association. In other words, the "criterion" of consistency is asymmetrical, like most of the other Bradford Hill "criteria".

This is relevant to the current position with EMF where consistent research results are not generally available. Such inconsistency is to be expected, particularly at this relatively early stage in the complex biological and physical story of EMF.

There is great scope for legitimate differences of view about this and other implications of the complexity, uncertainty and ignorance that characterise the EMF debate. Judgements need to be made, for example, about the weights to be placed on the presence or absence of features of the evidence, such as consistent research results, mechanisms of action, and animal evidence. There is therefore likely to be wide divergences of scientific opinions between different groups of scientists who evaluate the same stock of scientific knowledge during their risk assessments.

For example, in 2000, the UK National Radiological Protection Board set up the Stewart Committee to evaluate the evidence on mobile phones. It concluded that the evidence for safety was not great; that the evidence for harm was weak, but that this was to be expected at this early stage in the history of mobile phones; that the numbers of people, especially young people, exposed was widespread and rising; and that the precautionary principle was relevant, and justified the recommendation that mobiles phones ought not be used by children under 16, except in emergencies [5].

During the same year, a radiation advisory Committee under the Dutch Health Council, comprising similarly qualified scientists, evaluated the same stock of knowledge and concluded that the evidence for safety was robust; that the evidence for harm to RF exposure was largely absent; that children were not more sensitive to RF exposures from mobile phones than adults; and that the precautionary principle was not relevant: no action on exposure reduction was therefore justified [83].

In order to tease out the different and largely hidden assumptions and inferential rules adopted by the two committees, the EEA organised a workshop in May 2008 at which representatives of the two committees explained how they came to such divergent opinions. They were joined by scientists who had produced different evaluations of essentially the same knowledge in three other case studies: ELF from power lines; the plastics chemical, bisphenyl A; and pesticides spray drift.

A brief report summarising the EEA workshop, and containing an eighteen-point checklist that identifies the main reasons for such divergences of view is now available [84].

There appears to be very few risk assessments of EMF that are transparent about how their largely implicit assumptions, judgements and rules of inference affected their conclusions.

An exception is the Californian Department of Health Services evaluation of the possible risks from ELF power line exposures [60]. This report was transparent about its graduated approach to strengths of evidence, about the weights that the individual scientist involved in the assessment placed on different types of evidence, and their types of argumentation and their rules of inference. The assessment was longer and more resource consuming than other EMF risk assessments but its transparency, and stakeholder involvement in agreeing the approach to evaluating the evidence, seems to have produced a more socially and scientifically robust assessment. The recent report from the US National Academy of Sciences on Risk Assessment strongly recommends such transparency and stakeholder involvement, especially at the crucial problem framing stage [65].

13. Conclusion

The successful application of available scientific knowledge and of the precautionary principle to public policy-making on health and environment involves several issues that have been identified in, or have arisen from, debates over some late lessons from early warnings that the EEA has identified. Such issues include the contingent nature of knowledge; approaches to uncertainty, ignorance and "surprises"; appropriate strengths of evidence for policy actions; the biases in the environmental health sciences; public participation in risk analysis and in choices over innovation pathways: and the need for more realism and transparency in the evaluation of evidence about complex ecological and biological realities.

These issues are particularly relevant to the potential hazards that are now emerging from, inter alia, nanotechnology, where scientific ignorance predominates [85]; from the non-ionising radiations arising from the use of mobile phones and power lines; and from endocrine disrupting substances. Such issues require new approaches that, inter alia, involve elements of what has been called post normal science [86].

The capacity of "homo sapiens" (who should perhaps be called, with less hubris, "homo stupidus" as few, if any other species, consciously destroy their habitats) to foresee and forestall disasters, appears to be limited, as the EEA reports on late lessons illustrate.

Societies could, however, with more humility in the face of uncertainty and ignorance, heed the late lessons and, aided by a wider, yet wise application of the precautionary principle, anticipate and minimise hazards. In so doing they would stimulate more participatory risk analysis and governance; the use of more realistic and transparent systems science; and the development of more socially robust and technologically diverse technological and social innovations.

Three main scenarios seem to face us with EMF, particularly with the RF from mobile phones. The first is similar to the case studies in the EEA reports on late lessons, where much avoidable harm was not prevented. The second is where precautionary actions to reduce EMF exposures avert much potential harm, whilst stimulating more sustainable innovation in the production and use of mobile phone technologies and energy systems. And the third is where such precautionary actions to reduce exposures are taken but they turn out to have been unnecessary, if reasonable, given the state of knowledge today. The choice is ours: to act or not to act, as Shakespeare might have said.

Disclaimer

The views expressed are those of the author and do not represent the views of the EEA or its Management Board. The author has no competing financial interest in the matters dealt with.

References

[1] EEA, "Late Lessons from Early Warnings: The Precautionary Principle 1896–2000", European Environment Agency, Copenhagen, Denmark, 2001.

[2] I. Aslaksen, B. Natwig, I. Nordal, Environmental risk and the precautionary principle: "Late Lessons from Early Warnings applied to Genetically Modified Plants", J. Risk Res. 9 (3) (2006) 205–224.

[3] T. Traavik, L. Li Ching, Biosafety First: Holistic approaches to Risk and Uncertainty in Genetic Engineering and Genetically Modified Organisms", Tapir Academic Press, 2007.

[4] Royal Society, Nanoscience and Nanotechnologies: Opportunities and Uncertainties, London, 2003. Available from: <http://www.nanotec.org.uk/finalReport.htm>.

[5] T. Stewart, Report on mobile phones and health, IEGMP, NRPB, 2000. Available from: <http://www.iegmp.org.uk/report/text.htm>.

[6] Mobile Phones and Health, IEGMP Reports, NRPB, 2004. Available from: <http://www.hpa.org.uk/radiation/publications/documents_of_nrpb/pdfs/doc_15_5.pdf>.

[7] WHO, Global Assessment of the State-of-the-Science of Endocrine Disruptors, World Health Organization, Geneva, 2002. Available from: <http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/print.html>.

[8] D. Gee, Late lessons from early warnings: towards realism and precaution with endocrine disrupting substances, Environ. Health Perspect. 114 (Suppl. 1) (2006) 152–160.

[9] Chemtrust, Effects of Pollutants on the Reproductive Health of Male Vertebrate Wildlife Males Under Threat, Gwynne Lyons, London, 2008.

[10] J. Graham, Europe's Precautionary Principles: promise and pitfalls, J. Risk Res. 5 (4) (2002) 375.

[11] M. Planck, Scientific Autobiography and Other Papers, Philosophical Library, New York, 1949.

[12] IPPC, Uncertainty Guidance note for authors of the Fourth Assessment report, Geneva, 2005.

[13] ICNIRP, Guidelines for limiting exposures to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz), Health Physics, 74, Nos. 494–522, 1998, p. 496.

[14] J. Swanson, L. Kheifets, Biophysical mechanisms: a component in the weight of evidence for health effects of power frequency electric and magnetic fields, Rad. Res. 165 (2006) 470–478.

[15] WHO, Environmental Health Criteria 238, Extremely Low Frequency Fields, 2007.

[16] W.R. Adey, Potential therapeutic applications of non-thermal electromagnetic fields: ensemble organisation of cells in tissue as a factor in

biological field sensing, in: P.J. Rosch, M.S. Markov (Eds.), Bioelectromagnetic Medicine, 2004.
[17] C. Brauner, Electrosmog—a Phantom Risk, Swiss Re.
[18] D.L. Henshaw, M.J. O'Carroll, Response to Draft Opinion of SCENIHR on EMF, University of Bristol, 2006.
[19] M. Blank, Health Risk of Electromagnetic Fields: Research on the Stress Response, in Bioinitiative Report: a Rationale for a Biologically based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. Available from: <http://www.bioinitiative.org>.
[20] T. Kuhn, The Structure of Scientific Revolutions, University of Chicago Press, 1962.
[21] O'Carroll, Application of the Precautionary Principle to EMF, Paper to the WHO/EC/NIEHS Workshop, Luxembourg, 24–26th February 2003.
[22] D.L. Henshaw, R.J. Reiter, Do magnetic fields cause increased risk of childhood leukemia via melatonin disruption? A review, Bioelectromagn. Suppl. 7 (2005) S86–S97.
[23] Swedish Environmental Protection Agency, 4th Report on EMF, 2007, p. iii.
[24] IARC, Non-ionising radiation. Part 1. Static and extremely low frequency (ELF) electric and magnetic fields, in: International Agency for Research on Cancer Monographs on the evaluation of carcinogenic risks to humans, Lyon, vol. 80, 2002.
[25] X. Shen, Y. Yang, X. Jin, C. Yan, Y. Tian, J. Tang, Case-only study of interactions between DNA repair genes (*hMLH1*, *APEX1*, *MGMT*, *XRCC1* and *XPD*) and low-frequency electromagnetic fields in childhood acute leukaemia, Leukemia Lyphoma (December) (2008).
[26] B. Lambert, Radiation: Early Warnings, Late Effects, Chapter 3 in Late Lessons from Early Warnings, EEA, 2001.
[27] SCENIHR, Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), Opinion on Possible Effects of Electromagnetic Fields (EMF) on Human Health, March 2007. Available from: <http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_007.pdf>.
[28] The Controversy about a Possible relationship between Mobile Phone Use and Cancer, Environmental Health Perspectives online, 26 September 2008.
[29] L. Hardell, M. Carlberg, F. Sodrqvist, K.H. Mild, Meta-analysis of long term mobile phone use and the association with brain tumours, Int. J. Oncol. 32 (2008) 1097–1103.
[30] L.E. Edqvist, K.B. Pedersen, Antimicrodials as Growth Promotors: resistance to Common Sense, Chapter 9 in Late Lessons from Early Warnings, EEA, 2001.
[31] M.M. Swann Report, Joint Committee on the use of Antibiotics in Animal Husbandry and Veterinary Medicine, HMSO, London, 1969.
[32] Case T-13/99 Pfizer ECR II-3305 and in Case T-70/99, Alpharma, ECR, II-3495, September 11, 2002.
[33] Bioinitiative Report: a Rationale for a Biologically based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. Available from: <http://www.bioinitiative.org>.
[34] EEA, Radiofrequency Electromagnetic Fields: EEA Commentary on the Evaluation of the Evidence, March; EEA web item September 17th 2007, Radiation Risk from everyday devices assessed, Copenhagen (2007/08).
[35] N. Stern, The Economics of Climate Change, UK Treasury, 2006.
[36] BCPT, Special Issue on Prenatal Programming and Toxicity, in: P. Grandjean (Guest Ed.), Basic and Clinical Pharmacology & Toxicology, 102, No. 2, February 2008.
[37] Grandjean et al., The Faroes Statement: Human Health Effects of Developmental Exposure to Chemicals in Our Environment, in BCPT, 2008.
[38] D. Gee, Establishing Evidence for Early Action: the prevention of reproductive and developmental harm, Basic Clin. Pharmacol. Toxicol. 102 (2) (2008) 257–266.
[39] Plato's Apology 1.21, "So I am likely to be wiser than he to this small extent, that I do not think I know what I do not know.".
[40] D. Brewster (Ed.), Memoirs of Newton, vol. 2, 1855 (Chapter 27).
[41] A. Stirling, On science and precaution in the management of technological risk. Final summary report Technological Risk and Uncertainty project, European Scientific Technology Observatory, EC Forward Studies Unit, Brussels, 1999.
[42] D. Orrell, The Future of Everything; the Science of Prediction, Thunder's Mouth Press, New York, 2007.
[43] N.N. Taleb, The Black Swan: the Impact of the Highly Improbable, Penguin, 2008.
[44] D. Santillo, P. Johnston, W.J. Langston, Tributyltin (TBT) antifoulants: a tale of ships, snails and imposex, chapter 13 in Late Lessons from Early warnings, EEA, 2001.
[45] M. Stroebe, M. Scheringer, K. Hungerbuhler, Measures of overall persistence and the temporal remote state, Environ. Sci. Technol. 38 (2004) 5665–5673.
[46] UN, World Charter for Nature, UN General Assembly 37th Session (UN/GA/RES/37/ 7), New York, 1982.
[47] Marine Pollution Bulletin 34 (9) (1997) 680–681.
[48] A. Trouwborst, The Precautionary Principle in General International Law: Combating the Babylonian Confusion, RECEIL 16 (2) (2007) 185–195.
[49] Treaty establishing the European Community (consolidated text), Official Journal C 325 of 24 December 2002. Available from: <http://europa.eu.int/eur-lex/lex/en/treaties/dat/12002E/pdf/12002E_EN.pdf>.
[50] N. De Sadeleer, Implementing the Precautionary Principle: Approaches from the Nordic Countries, EU, and USA, Earthscan.
[51] A. Bradford Hill, The environment and disease: association or causation? in: Proceedings of the Royal Society of Medicine, vol. 58, 1965, pp. 295–300.
[52] General Food Law regulation, EC No. 178/2002, Official Journal of the EU, L31, 0.02.2002, Luxembourg.
[53] T. Christoforou, Science, law and precaution in dispute resolution on health and environmental protection: what role for scientific experts?, in: Le commerce international des organisms genetiquement modifies, Centre d'Etudes et de Recherches Internationales et Communautaires, Universite d'Àix-Marseille, 2002, p. 111.
[54] WHO, Declaration of Fourth Ministerial Conference on Environment and Health, Budapest, Hungary, 23–25 June 2004. Available from: <http://www.euro.who.int/document/e83335.pdf>.
[55] WHO, Dealing with uncertainty – how can the precautionary principle help protect the future of our children? Working paper for the Fourth Ministerial Conference on Environment and Health, Budapest, Hungary, 23–25 June 2004. Available from: <http://www.euro.who.int/document/hms/edoc11.pdf>.
[56] Health Council of the Netherlands, Prudent Precaution, 2008.
[57] European Commission, Communication from the Commission on the Precautionary Principle, COM, Brussels, 2000, p. 1.
[58] V.J. Cogliano, The IARC Monographs: a resource for Precaution and Prevention, a Commentary on the Editorial by Martuzzi on "The Precautionary Principle: in Action for Public Health", 2007, pp. 569–574. Available from: <http://oem.bmj.com>.
[59] IPCC, Intergovernmental Panel on Climate Change, Second, Third, and Fourth Assessment Reports, 1995, 2001, 2007. Available from: <http://www.ipcc.ch/pub/reports.htm>.
[60] R. Neutra, in: P.M. Wiedemann, H. Schutz (Eds.), Lessons from the California Electromagnetic Field Risk Assessment of 2002, The role of evidence in Risk Characterisation: Making sense of Conflicting Data, Wiley–VCH, Germany, 2007.
[61] US Presidential/Congressional Commission on Risk Assessment & Risk Management, Framework for Environmental Health Risk Assessment, Final Report, vol. 1, 1997. Available from: <http://www.riskworld.com/Nreports/1997/risk-rpt/pdf/EPAJAN.PDF>, Management.
[62] Royal Commission on Environmental Pollution Environmental Standards, The Stationary Office, London, 1998.
[63] German Advisory Council on Global Change, Strategies for Managing Global Environmental Risks, 2001.

[64] Codex Alimentarius Commission, Principles for Risk Analysis for Food Safety, FAO/WHO, Rome, 2007.
[65] NAS, Science and Decisions: Advancing Risk Assessment, Washington, 2008. Available from: <http://www.nap.edu/catalog/12209.html>.
[66] E. Millstone et al., JRC/IPTS, Risk Assessment Policies: Differences across jurisdictions, EU Joint Research Centre, Institute for Prospective Technological Studies, Seville, 2007.
[67] T. Christoforou, The precautionary principle and democratising expertise: a European legal perspective, Science and Public Policy 30, Surrey, England, No. 3, June 2003, pp. 205–221.
[68] J. Wilsdon, R. Willis, See-through Science – Why Public Engagement needs to Move Upstream, Demos, London, 2004.
[69] Wynne et al., Taking European Knowledge Society Seriously, Report of the Expert Group on Science and Governance to the Science, Economy and Society Directorate, Directorate-General for Research, European Commission, 2007.
[70] A. Pereira, S.G. Vaz, S. Tognetti (Eds.), Interfaces between Science and Society, Greenleaf Publishing.
[71] Netherlands Environmental Assessment Agency, Stakeholder Participation Guidance, Main Document, 2008.
[72] M. O'Carroll, Precautionary approaches and the SAGE experience, paper to Radiation Research Trust Conference: EMF and Health – A Global Issue, London, 8–9 September 2008.
[73] A. Mazur, True Warnings and False Alarms. Evaluating Fears about the Health Risks of Technology, 1948–1971, Resources for the Future, Washington, 2004.
[74] S.F. Hansen, M.P. Krayer von Krauss, J. Tickner, Categorising Mistaken False Positives in Regulation of Human and Environmental Health Risk Anal. 27 (1) (2007).
[75] P. Grandjean, M. Soffriti, F. Minardi, J. Brazier, The Precautionary Principle: Implications for Research and Prevention in Environmental and Occupational Health European Journal of Oncology Library, vol. 2, European Ramazzini Foundation, Bologna, Italy, 2003.
[76] Max Planck, Lecture on the Law of Causality and Free Will, February 1927.
[77] WHO, Extremely Low Frequency Fields, Environmental Health Criteria, No. 238, WHO, 2007, p. 274.
[78] D. Ibarreta, S.H. Swann, The DES story: long term consequences of prenatal exposure, Chapter 8 in Late Lessons from Early Warnings, EEA, 2001.
[79] P. Vineis, A self-fulfilling prophecy: are we underestimating the role of the environment in gene–environment interaction research? Int. J. Epidemiol. 33 (2004) 945–946.
[80] C.F. Sing, J.H. Stengard, S.L.R. Kardia, Dynamic relationships between the Genome and Exposures to environments as causes of common human diseases, Chapter in Nutrigenetics and Nutrigenomics World Review of Nutrition and Diet, Basel, Karger, vol. 93, 2004, pp. 77–91.
[81] US National Academy of Sciences, Cumulative Risk Assessment of Phthalates and Related Chemicals, National Academy of Sciences, 87 US Surgeon General (1964), Smoking and Health, Department of Health and Human Sciences, Washington, 2008.
[82] H.L. Needleman, Making Models of Real World events: the use and abuse of inference, Neurotoxicol. Teratol. 17 (3) (1995).
[83] Health Council of the Netherlands, Mobile Phones: an Evaluation of Health Effects, 2002.
[84] EEA, paper summarizing the workshop on Evaluating Evidence, Copenhagen, May 2008.
[85] Royal Commission on Environmental Pollution, Novel Materials in the Environment: the Case of Nanotechnology, The Stationary Office, London, 2008.
[86] S. Funtowicz, J. Ravetz, in: S. Krimsky, D. Golding (Eds.), Three Types of Risk Assessment and the Emergence of Post-Normal Science: In Social Theories of Risk, Praeger, Westport, 1992, pp. 251–273.

ELSEVIER

Pathophysiology 16 (2009) 233–246

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

Public health implications of wireless technologies

Cindy Sage[a,*], David O. Carpenter[b]

[a] *Sage Associates, 1396 Danielson Road, Santa Barbara, CA 93108, USA*
[b] *Institute for Health and the Environment, University at Albany, Rensselaer, NY, USA*

Received 18 January 2008; accepted 30 January 2009

Abstract

Global exposures to emerging wireless technologies from applications including mobile phones, cordless phones, DECT phones, WI-FI, WLAN, WiMAX, wireless internet, baby monitors, and others may present serious public health consequences. Evidence supporting a public health risk is documented in the BioInitiative Report. New, biologically based public exposure standards for chronic exposure to low-intensity exposures are warranted. Existing safety standards are obsolete because they are based solely on thermal effects from acute exposures. The rapidly expanding development of new wireless technologies and the long latency for the development of such serious diseases as brain cancers means that failure to take immediate action to reduce risks may result in an epidemic of potentially fatal diseases in the future. Regardless of whether or not the associations are causal, the strengths of the associations are sufficiently strong that in the opinion of the authors, taking action to reduce exposures is imperative, especially for the fetus and children. Such action is fully compatible with the precautionary principle, as enunciated by the Rio Declaration, the European Constitution Principle on Health (Section 3.1) and the European Union Treaties Article 174.
© 2009 Elsevier Ireland Ltd. All rights reserved.

Keywords: Wireless technology; Brain cancer; Radiofrequency; Cell phones; Wireless antenna facilities; Childrens' health

1. Introduction and background

Exposure to electromagnetic fields (EMF) has been linked to a variety of adverse health outcomes that may have significant public health consequences [1–13]. The most serious health endpoints that have been reported to be associated with extremely low frequency (ELF) and/or RF include childhood and adult leukemia, childhood and adult brain tumors, and increased risk of the neurodegenerative diseases, Alzheimer's and amyotrophic lateral sclerosis (ALS). In addition, there are reports of increased risk of breast cancer in both men and women, genotoxic effects (DNA damage and micronucleation), pathological leakage of the blood–brain barrier, altered immune function including increased allergic and inflammatory responses, miscarriage and some cardiovascular effects [1–13]. Insomnia (sleep disruption) is reported in studies of people living in very low-intensity RF environments with WI-FI and cell tower-level exposures [85–93]. Short-term effects on cognition, memory and learning, behavior, reaction time, attention and concentration, and altered brainwave activity (altered EEG) are also reported in the scientific literature [94–107]. Biophysical mechanisms that may account for such effects can be found in various articles and reviews [136–144].

The public health implications of emerging wireless technologies are enormous because there has been a very rapid global deployment of both old and new forms in the last 15 years. In the United States, the deployment of wireless infrastructure has accelerated greatly in the last few years with 220,500 cell sites in 2008 [14–16]. Eighty-four percent of the population of the US own cell phones [16]. Annualized wireless revenues in 2008 will reach $144 billion and US spending on wireless communications will reach $212 billion by 2008. Based on the current 15% annual growth rate enjoyed by the wireless industry, in the next 5 years wireless will become a larger sector of the US economy than both the agriculture and automobile sectors. The annualized use of cell phones in the US is estimated to be 2.23 trillion minutes in 2008 [16]. There are 2.2 billion users of cell phones worldwide in 2008 [17] and many million more users of cordless phones.

Over 75 billion text messages were sent in the United States, compared with 7.2 billion in June 2005, according to

* Corresponding author. Tel.: +1 805 969 0557; fax: +1 805 969 5003.
E-mail address: sage@silcom.com (C. Sage).

0928-4680/$ – see front matter © 2009 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.pathophys.2009.01.011

CTIA, the Wireless Association, the leading industry trade group [16]. The consumer research company Nielsen Mobile, which tracked 50,000 individual customer accounts in the second quarter of this year, found that Americans each sent or received 357 text messages a month then, compared with 204 phone calls. That was the second consecutive quarter in which mobile texting significantly surpassed the number of voice calls [17].

The Electronics Industries Alliance (EIA) represents 80% of the $550 billion US electronics industry "that provides two million jobs for American workers." Its members include companies from the consumer electronics and telecommunications industries, among others [17].

There is intense industry competition for market share. Telecom taxes form an immense revenue generator for the government sector. Sale of the airwaves (auctions selling off wireless bandwidth) is a multi-million dollar industry for governments, and multi-billion dollar global advertising budgets are common. Lobbying dollars from the telecom-related industries are estimated to be $300 million annually. The media is nearly silent on health issues, perhaps in part because of global advertising revenues that compromise journalistic independence and discourage balanced coverage of health, equity and economic issues.

2. Evidence supporting a public health risk

Even if there is only a small risk to health from chronic use of and exposure to wireless technologies, there is the potential for a profound public health impact. RF radiation now saturates the airwaves, resulting in exposure to both users and non-users. The effects are both short-term (sleep disruption, hormone disruption, impairment of cognitive function, concentration, attention, behavior, and well-being) and they are almost certainly long-term (generational impacts on health secondary to DNA damage, physiological stress, altered immune function, electrosensitivity, miscarriage risks, effects on sperm quality and motility leading to infertiility, increased rates of cancer, and neurological diseases including Alzheimer's disease and ALS—at least for ELF exposures). (Chapters 5–12 of the BioInitiative Report [1] and papers in this Supplement.)

There is credible scientific evidence that RF exposures cause changes in cell membrane function, metabolism and cellular signal communication, as well as activation of proto-oncogenes and triggering of the production of stress proteins at exposure levels below current regulatory limits. There is also generation of reactive oxygen species, which cause DNA damage, chromosomal aberrations and nerve cell death. A number of different effects on the central nervous system have also been documented, including activation of the endogenous opioid systems, changes in brain function including memory loss, slowed learning, motor dysfunction and performance impairment in children, and increased frequency of headaches, fatigue and sleep disorders. Melatonin secretion is reduced, resulting in altered circadian rhythms and disruption of several physiological functions. (Chapters 5–12 of the BioInitiative Report [1] and papers in this Supplement.)

These effects can reasonably be presumed to result in adverse health effects and disease with chronic and uncontrolled exposures, and children may be particularly vulnerable [1,19]. The young are also largely unable to remove themselves from such environments. Second-hand non-ionizing radiation, like second-hand smoke may be considered of public health concern based on the evidence at hand.

2.1. Malignant brain tumors

At present, the most persuasive evidence for cancer resulting from RF exposure is that there is a significantly increased risk of malignant glioma in individuals that have used a mobile phone for 10 or more years, with the risk being elevated only on the side of the head on which the phone is used regularly (ipsilateral use) [1,3,4,6–8,18]. While the risk for adults after 10 or more years of use is reported to be more than doubled, there is some evidence beginning to appear that indicates that the risk is greater if the individual begins to use a mobile phone at younger ages. Hardell et al. [18] reported higher odds ratios in the 20–29-year-old group than other age ranges after more than 5 years of use of either analog or cordless phones. Recently in a London symposium Hardell reported that after even just 1 or more years of use there is a 5.2-fold elevated risk in children who begin use of mobile phones before the age of 20 years, whereas for all ages the odds ratio was 1.4. Studies from Israel have found that the risk of parotid gland tumors (a salivary gland in the cheek) is increased with heavy cell phone use [7]. The risk of acoustic neuroma (a benign but space-occupying tumor on the auditory nerve) is also significantly increased on the ipsilateral side of the head after 10 or more years of mobile phone use [1,3]. This relationship has also been documented in some of the published reports of the WHO Interphone Study, a decade-long 13-country international assessment of cell phone risks and cancer [6,8].

Kundi reports that "(E)pidemiological evidence compiled in the last 10 years starts to indicate an increased risk, in particular for brain tumors (glioma, meningioma, acoustic neuroma), from mobile phone use. Considering biases that may have been operating in most studies the risk estimates are rather too low, although recall bias could have increased risk estimates. The net result, when considering the different errors and their impact is still an elevated risk" [19].

The latency for most brain tumors is 20 years or more when related to other environmental agents, for example, to X-ray exposure. Yet, for cell phone use the increased risks are occurring much sooner than twenty years, as early as 10 years for brain tumors in adults and with even shorter latencies in children. This suggests that we may currently be significantly underestimating the impact of current levels of

use of RF technology, since we do not know how long the average latency period really is. If it is 20 years, then the risk rate will likely be much higher than an overall doubling of risk for cell phone users if the peak comes later than 10 years. It may also signal very troubling risks for those who start using cell phones, and perhaps all wireless devices, in early childhood. We may not have proof of effect for decades until many hundreds of thousands of new cases of malignant gliomas are set in motion by long-term cell phone use.

The preliminary evidence that mobile phone use at younger ages may lead to greater risk than for older persons is of particular concern. There is a large body of evidence that childhood exposure to environmental agents poses greater risk to health than comparable exposure during adulthood [20,21]. There is reason to expect that children would be more susceptible to the effects of EMF exposure since they are growing, their rate of cellular activity and division is more rapid, and they may be more at risk for DNA damage and subsequent cancers. Growth and development of the central nervous system is still occurring well into the teenage years so that neurological changes may be of great importance to normal development, cognition, learning, and behavior.

A greater vulnerability of children to developing brain cancer from mobile phone use may be the consequence of a combination of patterns of use, stage of development and physical characteristics related to exposure. In addition to the fact that the brain continues to develop through the teen years, many young children and teenagers now spend very large periods of time using mobile phones. The brain is the main target organ of cell phones and cordless phones, with highest exposure to the same side as the phone is used. Further, due to anatomical reasons, the brain of a child is more exposed to RF radiation than the brain of an adult [22,23]. This is caused by the smaller brain size, a thinner pinna of the ear, thinner skin and thinner skull bone permitting deeper penetration into the child's brain. A recent French study showed that children absorb twice the RF from cell phone use as do adults [24].

In addition to concerns about cancer, there is evidence for short-term effects of RF exposure on cognition, memory and learning, behavior, reaction time, attention and concentration, altered brainwave activity (altered EEG) [95–108], and all of these effects argue for extreme caution with regard to exposure of children. The development of children into adults is characterized by faster cell division during growth, the long period needed to fully develop and mature all organ systems, and the need for properly synchronized neural development until early adulthood. Chronic, cumulative RF exposures may alter the normal growth and development of children and adversely affect their development and capacity for normal learning, nervous system development, behavior and judgment [1,97,102].

Prenatal exposure to EMF has been identified as a possible risk factor for childhood leukemia (1). Maternal use of cell phones has been reported to adversely affect fetal brain development, resulting in behavioral problems in those children by the time they reach school age [25]. Their exposure is involuntary in all cases. Children are largely unable to remove themselves from exposures to harmful substances in their environments.

2.2. *Plausible biological mechanisms for a relationship between RF exposure and cancer*

2.2.1. *DNA damage and oxidative stress*

Damage to DNA from ELF and from RF cell phone frequencies at very low intensities (far below FCC and ICNIRP safety limits) has been demonstrated in many studies [1,2,26–35]. Both single- and double-strand DNA damage have been reported by various researchers in different laboratories. This is damage to the human genome, and can lead to mutations which can be inherited, or which can cause cancer, or both.

Non-ionizing radiation is assumed to be of too low energy to cause direct DNA damage. However both ELF and RF radiation induce reactive oxygen species, free radicals that react with cellular molecules including DNA. Free-radical production and/or the failure to repair DNA damage (secondary to damage to the enzymes that repair damage) created by such exposures can lead to mutations. Whether it is greater free-radical production, reduction in anti-oxidant protection or reduced repair capacity, the result will be altered DNA, increased risk of cancer, impaired or delayed healing, and premature aging [36–54]. Exposures have also been linked to decreased melatonin production, which is a plausible biological mechanism for decreased cancer surveillance in the body, and increased cancer risk [34,39,44,46,47,49,50,54]. An increased risk of cancers and a decrease in survival has been reported in numerous studies of ELF and RF [55–69].

2.2.2. *Stress proteins (heat shock proteins or HSP)*

Another well-documented effect of exposure to low-intensity ELF and RF is the creation of stress proteins (heat shock proteins) that signal a cell is being placed under physiological stress) [70–80]. The HSP response is generally associated with heat shock, exposure to toxic chemicals and heavy metals, and other environmental insults. HSP is a signal of cells in distress. Plants, animals and bacteria all produce stress proteins to survive environmental stressors like high temperatures, lack of oxygen, heavy metal poisoning, and oxidative stress.

We can now add ELF and RF exposures to this list of environmental stressors that cause a physiological stress response. Very low-level ELF and RF exposures can cause cells to produce stress proteins, meaning that the cell recognizes ELF and RF exposures as harmful. This is another important way in which scientists have documented that ELF and RF exposures can be harmful, and it happens at levels far below the existing public safety standards. An additional concern is that if the stress goes on too long, the protective effect is diminished. The reduced response with prolonged exposure means the cell is less protected against

damage, and this is why prolonged or chronic exposures may be harmful, even at very low intensities.

2.2.3. RF-induced gene expression changes

Many environment agents cause diseases, including cancer, not by direct damage to DNA but rather by up- or down-regulation of genes that regulate cell growth and function. Usually there are many genes whose expression is changed, and it is difficult to determine the exact changes responsible for the disease. Both ELF and RF exposures have been shown to result in altered gene expression. Olivares-Banuelos et al. [81] found that ELF exposure of chromaffin cells resulted in changed expression of 53 transcripts. Zhao et al. [82] investigated the gene expression profile of rat neurons exposed to 1800 MHz RF fields (2 W/kg) and found 24 up-regulated genes and 10 down-regulated genes after a 24-h exposure. The altered genes were involved in multiple cellular functions including cytoskeleton, signal transduction pathways and metabolism. Kariene et al. [83] exposed human skin to mobile phone radiation, and found by punch biopsy that 8 proteins were significantly altered in expression, consistent with gene induction. Several other studies have found altered gene expression following RF exposure, although none have been found that explain specific disease states [84].

DNA activation at very low ELF and RF levels, as in the stress response, and DNA damage (strand breaks and micronuclei) at higher levels, are molecular precursors to changes that are believed to lead to cancer. These, along with gene induction, provide plausible biological mechanisms linking exposure to cancer.

The biochemical pathways that are activated are the same for ELF and for RF exposures, and are non-thermal (do not require heating or induced electrical currents). This is true for the stress response, DNA damage, generation of reactive oxygen species as well as gene induction. Thus it is not surprising that the major cancers resulting from exposure to ELF and RF are the same, namely leukemia and brain cancer. The safety standards for both ELF and RF, based on protection from heating, are irrelevant and not protective. ELF exposure levels of only 5–10 mG have been shown to activate the stress response genes (http://www.bioinitiative.org, Sections 1 and 7 [1]).

3. Sleep, cognitive function and performance

The relationship of good sleep to cognition, performance and healing is well recognized. Sleep is a profoundly important factor in proper healing, anti-inflammatory benefits, reduction in physical symptoms of such as tendonitis, over-use syndrome, fatigue-induced lethargy, cognition and learning. Incomplete or slowed physiological recovery is common when sleep is impaired. Circadian rhythms that normalize stress hormone production (cortisol, for example) depend on synchronized sleep patterns.

People who are chronically exposed to low-level wireless antenna emissions report symptoms such as problems in sleeping (insomnia), as well as other symptoms that include fatigue, headache, dizziness, grogginess, lack of concentration, memory problems, ringing in the ears (tinnitus), problems with balance and orientation, and difficulty in multi-tasking [85–93,99]. In children, exposures to cell phone radiation have resulted in changes in brain oscillatory activity during some memory tasks [97,102]. Cognitive impairment, loss of mental concentration, distraction, speeded mental function but lowered accuracy, impaired judgment, delayed reaction time, spatial disorientation, dizziness, fatigue, headache, slower motor skills and reduced learning ability in children and adults have all been reported [85–108].

These symptoms are more common among "electrosensitive" individuals, although electrosensitivity has not been documented in double-blind tests of individual identifying themselves as being electrosensitive as compared to controls [109,110]. However people traveling to laboratories for testing are pre-exposed to a multitude of RF and ELF exposures, so they may already be symptomatic prior to actual testing. There is also evidence that RF exposures testing behavioral changes show delayed results; effects are observed after termination of RF exposure. This suggests a persistent change in the nervous system that may be evident only after time has passed, so is not observed during a short testing period.

3.1. Plausible biological mechanisms for neurobehavioral effects

3.1.1. The melatonin hypothesis

While there remains controversy as to the degree that RF and ELF fields alter neurobehavioral function, emerging evidence provides a plausible mechanism for both effects on sleep and cognition. Sleep is controlled by the central circadian oscillator in the suprachiasmatic nucleus, located in the hypothalamus. The activity of this central circadian oscillator is, in turn, controlled by the hormone, melatonin, which is released from the pineal gland [111]. There is considerable evidence that ELF exposure reduces the release of melatonin from the pineal gland—see Section 12 of the Bioinitiative Report [1]. There has been less study of the effects of RF exposure on melatonin release, but investigations have demonstrated a reduced excretion of the urinary metabolite of melatonin among persons using a mobile phone for more than 25 min per day [112]. In a study of women living near to radio and television transmitters, Clark et al. [113] found no effect on urinary melatonin metabolite excretion among pre-menopausal women, but a strong effect in post-menopausal women.

The "melatonin hypothesis" also provides a possible basis for other reported effects of EMFs. Melatonin has important actions on learning and memory, and inhibits electrophysiological components of learning in some but not all areas of the brain [114,115]. Melatonin has properties as a free-radical scavenger and anti-oxidant [116], and consequently,

a reduction in melatonin levels would be expected to increase susceptibility to cancer and cellular damage. Melatonin could also be the key to understanding the relationship between EMF exposure and Alzheimer's disease. Noonan et al. [117] reported that there was an inverse relationship between excretion of the melatonin metabolite and the 1–42 amino acid form of amyloid beta in electric utility workers. This form of amyloid beta has been found to be elevated in Alzheimer's patients.

3.1.2. Blood–brain barrier alterations

Central nervous system effects of EMFs may also be secondary to damage to the blood–brain barrier (BBB). The blood–brain barrier is a critical structure that prevents toxins and other large molecules that are in peripheral blood from having access to the brain matter itself. Salford et al. [118] have reported that a 2-h exposure of rats to GSM-900 radiation with a SAR of 2–200 mW/kg resulted in nerve cell damage. In a follow-up study, Eberhardt et al. report that 2-h exposures to cell phone GSM microwave RF resulted in leakage of albumin across the blood–brain barrier and neuronal death [119]. Neuronal albumin uptake was significantly correlated to occurrence of damaged neurons when measured at 28 days post-exposure. The lowest exposure level was 0.12 mW/kg (0.00012 W/kg) for 2 h. The highest exposure level was 120 mW/kg (0.12 W/kg). The weakest exposure level showed the greatest effect in opening the BBB [118]. Earlier blood–brain studies by Salford and Schirmacher [120,121] report similar effects.

4. What are sources of wireless radiation?

There are many overlapping sources of radiofrequency and microwave emissions in daily life, both from industrial sources (like cell towers) and from personal items [cell and cordless phones, personal digital assistants (PDAs), wireless routers, etc.]. Published data on typical levels found in some cities and from some sources are available at http://www.bioinitiative.org [1,122–124].

Cell phones are the single most important source of radiofrequency radiation to which we are exposed because of the relatively high exposure that results from the phone being held right against the head. Cell phones produce two types of emissions that should be considered. First, the radiofrequency radiation (typically microwave frequency radiation) is present. However, there is also the contribution of the switching battery pack that produces very high levels of extremely low frequency electromagnetic field [125–127].

Cordless telephones have not been widely recognized as similar in emissions to cell phones, but they can and do produce significant RF exposures. Since people tend to use them as substitutes for in-home and in-office corded or traditional telephones, they are often used for long periods of time. As the range of cordless phones has increased (the distance away that you can carry on a conversation is related to the power output of the phone), the more powerful the RF signal will be. Hence, newer cordless phones may in some cases be similar to the power output of cell phones. The cumulative emissions from cell and cordless phones taken together should be recognized when considering the relative risks of wireless communication exposures.

PDAs such as the BlackBerry, Treo and iPhone units are 'souped-up' versions of the original voice communication devices (cell phones). The often produce far higher ELF emissions than do cell phones because they use energy from the battery very intensively for powering color displays and during data transmission functions (email, sending and receiving large files, photos, etc.) [125–127]. ELF emissions have been reported from PDAs at several tens to several hundreds of milligauss. Evidence of significantly elevated ELF fields during normal use of the PDA has public health relevance and has been reported in at least three scientific papers [125,128,129]. In the context of repetitive, chronic exposure to significantly elevated ELF pulses from PDAs worn on the body, relevant health studies point to a possible relationship between ELF exposure and cancer and pregnancy outcomes [130–133].

We include discussion of the ELF literature for two reasons. As mentioned above ELF activates the same biology as RF, it contributes to the total EMF burden of the body. In addition, PDAs and cell phones emit both radiofrequency/microwave radiation (RF) and extremely low frequency ELF from the battery switching of the device (the power source). Studies show that some devices produce excessively high ELF exposures during voice and data transmission. ELF is already classified as a 2B (Possible) Carcinogen by IARC, which means that ELF is indisputably an issue to consider in the wireless technology debate. ELF has been classified as a Group 2B carcinogen for all humans, not just children. The strongest evidence came from epidemiological studies on childhood leukemia, but the designation applies to all humans, both adults and children [1,25].

Wireless headsets that allow for conversations with cell phones at a distance from the head itself reduce the emissions. Depending on the type of wireless device, they may operate (transmit signal) only during conversations or they may be operational continuously. The cumulative dose of wireless headsets has not been well characterized under either form of use. Substantial cumulative RF exposure would be expected if the user wears a wireless headset that transmits a signal continuously during the day. However a critical factor is where the cell phone is placed. If worn on a belt with a headset, the exposure to the brain is reduced but the exposure to the pelvis may be significant.

Cell towers (called "masts" in Europe and Scandinavian countries) are wireless antenna facilities that transmit the cell phone signals within communities. They are another major source of RF exposures for the public. They differ from RF exposures from wireless devices like cell phones in that they produce much lower RF levels (generally 0.05 to 1–2 $\mu W/cm^2$ in the first several hundred feet around them) in comparison to several hundred microwatts per centimeter

squared for a cell phone held at the head. However they create a constant zone of elevated RF for up to 24 h per day. many hours per day, and the exposure is whole body rather than localized at the head. These facilities are the distribution system for wireless voice communications, internet connections and data transmission within communities. They are often erected on free-standing towers. They may be constructed on telephone poles or electrical poles. They may be built into the façade or rooftops of buildings behind wood screening. These are called stealth installations for wireless antenna facilities. Some installations are camouflaged to resemble 'false trees or rocks'. They emit RF to provide cell service to specific "cells" or locations that receive the signal.

Other forms of wireless transmission that are common in areas providing cell service are wireless land area networks (WLAN), (WiMAX) and WIFI networks. Some cities are installing city-wide WIFI service to allow any user on the street to log into the internet (without cables or wire connections). WIFI installations may have a signal reach for a few hundred feet where WiMAX installations may transmit signal more than 10 miles, so produce a stronger RF emission for those in close proximity. Each type has its particular signal strength and intended coverage area, but what they have in common is the production of continuous RF exposure for those within the area. We do not know what the cumulative exposure (dose) might be for people living, working or going to school in continuously elevated RF fields, nor are the possible health implications yet known. However, based on studies of populations near cell sites in general, there is a constellation of generally observed health symptoms that are reported to occur [85–107]. In this regard it is important to note that children living near to AM radio transmitters have been found to elevated risks of leukemia [134,135]. While AM radio RF fields are lower in frequency than that common in mobile phones, this is a total body irradiation with RF. The fact that leukemia, not brain cancer, is apparent in these studies suggests that leukemia is the cancer seen at the lowest levels of both ELF and RF fields under the circumstances of whole-body exposure.

Commercial surveillance systems or security gates pose an additional source of strong RF exposures. They are ubiquitous in department stores, markets and shops at the entry and exit points to discourage shoplifting and theft of goods. Security gates can produce excessively high RF exposures (although transitory) and have been associated with interference with pacemakers in heart patients. The exposure levels may approach thermal public safety limits in intensity, although no one expects a person to stand between the security gate bars for more than 6 min (safety limits for uncontrolled public access are variable depending on the frequency, but are all averaged over a 6-min exposure period).

RFID chips (radiofrequency identification chips) are being widely used to track purchases and for security of pets, and in some cases to keep track of patients with Alzheimer's disease and of children. RFID chips are implanted in fabrics, inserted in many types of commercial goods, and can be implanted under the skin. They create a detectable signal to track the location of people and goods.

5. Problems with existing public health standards (safety limits)

If the existing standards were adequate none of the effects documented above should occur at levels to which people are regularly exposed. The fact that these effects are seen with our current ambient levels of exposure means that our existing public safety standards are obsolete. It also means that new, biologically based public exposure standards for wireless technologies are urgently needed. Whether it is feasible to achieve low enough levels that still work and also protect health against effects of chronic RF exposure – for all age groups – is uncertain. Whether we can protect the public and still allow the kinds of wireless technology uses we see today is unknown.

The nature of electromagnetic field interactions with biological systems has been well studied [136–144]. For purposes of standard-setting processes for both ELF and RF, the hypothesis that tissue damage can result only from heating is the fundamental flaw in the misguided efforts to understand the basic biological mechanisms leading to health effects.

The thermal standard is clearly untenable as a measure of dose when EMF stimuli that differ by many orders of magnitude in energy can stimulate the same biological response. In the ELF range, the same biological changes occur as in the RF, and no change in temperature can even be detected. With DNA interactions the same biological responses are stimulated in ELF and RF ranges even though the frequencies of the stimuli differ by many orders of magnitude. The effects of EMF on DNA to initiate the stress response or to cause molecular damage reflect the same biology in different frequency ranges. For this reason it should be possible to develop a scale based on DNA biology, and use it to define EMF dose in different parts of the EM spectrum. We also see a continuous scale in DNA experiments that focus on molecular damage where single and double strand breaks have long been known to occur in the ionizing range, and recent studies have shown similar effects in both ELF and RF ranges [144].

Existing standard-setting bodies that regulate wireless technologies, assume that there are no bioeffects of concern at exposure levels that do not cause measurable heating. However, it has been established beyond any reasonable doubt that bioeffects and some adverse health effects occur at far lower levels of RF and ELF exposure where no heating (or induced current) occurs; some effects are shown to occur a thousand times or more below the existing public safety limits. New, biologically based public exposure limits are urgently needed. New wireless technologies for cell and cordless phones, other wireless communication and data transmission systems affect living organisms in new ways that our antiquated safety limits have not foreseen, nor protected against.

The exposure of children to electromagnetic fields has not been studied extensively; in fact, the Federal Communications Commission (FCC) standards for exposure to radiofrequency radiation are based on the height, weight and stature of a 6-foot tall man, not scaled to children or adults of smaller stature. They do not take into account the unique susceptibility of growing children to exposures, nor are there studies of particular relevance to children.

In addition there is a problem in the consideration of the level of evidence taken into consideration by these bodies. There have not been adequate animal models shown to have cancer as an endpoint, and a perception that no single mechanism is proven to explain these associations. Thus these committees have tended to ignore or minimize the evidence for direct hazard to humans, and believe there is no proof of cause and effect. These bodies assume from the beginning that only conclusive scientific evidence (absolute proof) will be sufficient to warrant change, and refuse to take action on the basis of a growing body of evidence which provides early but consequential warning of risks.

The Radiofrequency Interagency Working Group of the US governmental agencies involved in RF matters (RFIAWG) issued a Guidelines Statement in June of 1999 that concluded the present RF standard "may not adequately protect the public" [145]. The RFIAWG identified fourteen (14) issues that they believe are needed in the planned revisions of ANSI/IEEE RF exposure guidelines including "to provide a strong and credible rationale to support RF exposure guidelines". In particular, the RFIAWG criticized the existing standards as not taking into account chronic, as opposed to acute exposures, modulated or pulsed radiation (digital or pulsed RF is proposed at this site), time-averaged measurements that may erase the unique characteristics of an intensity-modulated RF radiation that may be responsible for reported biologic effects, and stated the need for a comprehensive review of long-term, low-level exposure studies, neurological-behavioral effects and micronucleus assay studies (showing genetic damage from low-level RF) [145]. This important document from relevant US agencies questions existing standards in the following ways: (a) selection of an adverse effect level for chronic exposures not based on tissue heating and considering modulation effects; (b) recognition of different safety criteria for acute and chronic exposures at non-thermal or low-intensity levels; (c) recognition of deficiencies in using time-averaged measurements of RF that does not differentiate between intensity-modulated RF and continuous wave (CW) exposure, and *therefore may not adequately protect the public*; (d) having standards based on adult males rather than considering children to be the most vulnerable group.

6. Prudent public health responses

Emerging environmental health problems require preventative public health responses even where scientific and medical uncertainties still exist, but where policy decisions today may greatly reduce human disease and societal costs tomorrow.

Policy decisions in public health must address some amount of uncertainty when balancing likely benefits and estimated costs. Although new insight will allow better appreciation of difficult issues, such as those occurring in environmental and occupational health, an expanded perspective may also enlarge the list of problems that need to be managed. Ignoring the problems carries its own costs (as deferring a decision is a decision in itself). With environmental and other public health problems becoming increasingly complex and international in scope, scientific documentation alone rarely justifies simple solutions [146].

Social issues regarding the controversy over public and occupational exposures to ELF and RF center on the resolute adherence to existing ICNIRP and FCC/IEEE standards by many countries, in the face of growing scientific evidence of health risks at far lower levels [10]. The composition of these committees, usually with excessive representation of the physics and engineering communities rather than public health professionals, results in a refusal to adopt biologically based exposure standards. Furthermore, there is widespread belief that governments are ignoring this evidence and there is widespread distrust of and lack of confidence in governments and their health agencies. The basis on which most review bodies and standard-setting agencies have avoided the conclusion that the science is strong enough to warrant new safety limits for ELF and RF is to require a demonstration of absolute proof before taking action. A causal level of evidence, or scientific certainty standard is implicit in nearly all reviews of the ELF and RF science, although this runs counter to good public health protection policies.

There is no question that global implementation of the safety standards proposed in the Bioinitiative Report, if implemented abruptly and without careful planning, have the potential to not only be very expensive but also disruptive of life and the economy as we know it. Action must be a balance of risk to cost to benefit. The major risk from maintaining the status quo is an increasing number of cancer cases, especially in young people, as well as neurobehavioral problems at increasing frequencies. The benefits of the status quo are expansion and continued development of communication technologies. But we suspect that the true costs of even existing technologies will only become much more apparent with time. Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior. Prudent corporate policies should be expected to address and avoid future risks and liabilities, otherwise, there is no market incentive to produce safe (and safer) products.

The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However, what has been missing with regard to EMF has been an acknowledgement of the risk that is demonstrated by

the scientific studies. There is clear evidence of risk, although the magnitude of the risk is uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society. New standards are warranted now, based on the totality of scientific evidence; the risks of taking no-action, the large population at risk, costs associated with ignoring the problem in new and upgraded site selection and construction, and the loss of public trust by ignoring the problem.

Direct medical and rehabilitative health costs associated with treatment for diseases that are reasonably related to wireless technologies may be very large. Although there is uncertainty involved in how much disease is related to wireless exposures, the mere scale of the problem with several billion users of cell phones and even larger impacts on bystander populations (from cell site exposures, from other WI-FI and wireless exposures in-home and commercial use, etc.) the associated public health costs will likely be monumental. Furthermore the costs to families with cancers, neurological diseases or learning disabilities in children related in part or in whole to wireless technologies extend beyond medical costs. They may reasonably extend to family disruption and family psychological problems, losses in job productivity and income loss.

The history of governments and their official health agencies to deal with emerging and newly identified risks to health is not good [147–149]. This is particularly true where industry investments in new products and technologies occur without full recognition, disclosure or even knowledge of possible health consequences. Large economic investments in polluting industries often make for perilously slow regulatory action, and the public health consequences may be very great as a result [150,151].

Free markets do not internalize the costs to society of "guessing wrong". Unexpected or hidden health costs of new technologies may not be seen for many years, when the ability to recall or to identify the precise exposures related to disease outcomes is difficult or impossible. The penalty nearly always falls to the individual, the family or the taxpayer and not to the industry that benefits economically—at least in free-market economies. Thus, the profits go to industry but the costs may go to the individual who can suffer both diminished quality of life and health and economic disadvantage. If all disease endpoints that may be reasonably related to chronic exposure to electromagnetic fields are considered even a small attributable fraction for one or more industries, it will have enormous global impact on public health. The public health implications are immense. But they can be reduced by strong government and public health interventions providing information on alternatives to wireless technologies, public education campaigns, health advisories, requirements for redesign of wireless devices, proscription of use of wireless devices by children and teenagers, strong and independent research programs on causes and prevention of EMF-related diseases, and consultation with all stakeholders on issues relating to involuntary exposures (bystander or second-hand radiation exposures from wireless technologies) (Table 1).

Table 1
Public health implications of wireless technologies argue for change in governmental and health agency actions.

Secure US and EU legislative mandates for safer technologies for communication and data transmission, for security and surveillance needs.
Promote wired alternatives for voice and data communication (cable, fiber-optic)
Discourage or ban use of cell phones by children and young teen-agers
Provide permanent (unremovable) labels on cell phones "Not for use by children under the age of 16"
Implement national public education campaigns on health issues (cell phones, cordless phones, PDAs, wireless internet, city-wide WI-FI, WLAN and WiMAX exposures
Promote industry redesign for safer products: support innovation for alternatives and solutions
Slow or stop deployment of wireless technologies to discourage reliance on wireless technologies for communication and security needs
Put the burden of proof on industry to show "new wireless tech" is safe before deployment
Adopt and enforce restricted use areas for sensitive or more vulnerable segments of society including low-EMF environments in public areas and "No Cell" zones in airports, hospitals, schools
Acknowledge FCC and ICNIRP thermal safety standards are obsolete for wireless technologies
Appoint new standard-setting bodies familiar with biological effects to develop new guidelines for public safety limits.
Develop new biologically based standards that address low-intensity, chronic exposures
Require standard of evidence and level of proof = public health
Reject "causal" standard of evidence for taking action on science
Make industry financially liable for "guessing wrong" and ignoring health risks

The scientific information contained in this Supplement argues for thresholds or guidelines that are substantially below current FCC and ICNIRP standards for localized exposures to wireless devices and for whole-body exposure. Uncertainty about how low such standards might have to go to be prudent from a public health standpoint should not prevent reasonable efforts to respond to the information at hand. No lower limit for bioeffects and adverse health effects from RF has been established, so the possible health risks of wireless WLAN and WI-FI systems, for example, will require further research. No assertion of safety at any level of wireless exposure (chronic exposure) can be made at this time. The lower limit for reported human health effects has dropped 100-fold below the safety standard (for mobile phones and PDAs); 1000–10,000-fold for other wireless (cell towers at distance; WI-FI and WLAN devices). The entire basis for safety standards is called into question, and it is not unreasonable to question the safety of RF at any level.

It is likely that for both ELF and RF, as for other carcinogens, there is no threshold of exposure that is without risk, but the magnitude of the risk increases linearly with the level of exposure. Our society will not go back to the pre-electric and pre-wireless age, but the clear evidence of health hazards to the human population from exposure mandates that we develop ways in which to reduce exposure through education, new technologies and the establishment of biomedically based standards.

7. Conclusions and recommended actions

New ELF limits are warranted based on a public health analysis of the overall existing scientific evidence. These limits should reflect environmental levels of ELF that have been demonstrated to increase risk for childhood leukemia, and possibly other cancers and neurological diseases. ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky. These levels are in the 2–4 milligauss (mG) range (0.2–0.4 μT), not in the 10 s of mG or 100 s of mG. The existing ICNIRP limit is 1000 mG (100 μT) and 904 mG (90.4 μT) in the US for ELF is outdated and based on faulty assumptions. These limits are can no longer be said to be protective of public health and they should be replaced. A safety buffer or safety factor should also be applied to a new, biologically based ELF limit, and the conventional approach is to add a safety factor lower than the risk level.

While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction. It is also recommended that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant (because of the possible link between childhood leukemia and *in utero* exposure to ELF). This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies. While it is not realistic to reconstruct all existing electrical distribution systems, in the short-term; steps to reduce exposure from these existing systems need to be initiated, especially in places where children spend time, and should be encouraged. These limits should reflect the exposures that are commonly associated with increased risk of childhood leukemia (in the 2–5 mG (0.2–0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Nearly all of the occupational studies for adult cancers and neurological diseases report their highest exposure category is 4 mG (0.4 μT) and above, so that new ELF limits should target the exposure ranges of interest, and not necessarily higher ranges.

Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

It is not prudent public health policy to wait any longer to adopt new public safety limits for ELF. These limits should reflect the exposures that are commonly associated with increased risk of childhood leukemia (in the 2–5 mG (0.2–0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

The rapid deployment of new wireless technologies that chronically expose people to pulsed RF at levels reported to cause bioeffects, which in turn, could reasonably be presumed to lead to serious health impacts, is a public health concern. There is suggestive to strongly suggestive evidence that RF exposures may cause changes in cell membrane function, cell communication, metabolism, activation of proto-oncogenes and can trigger the production of stress proteins at exposure levels below current regulatory limits. Resulting effects can include DNA breaks and chromosome aberrations, cell death including death of brain neurons, increased free-radical production, activation of the endogenous opioid system, cell stress and premature aging, changes in brain function including memory loss, retarded learning, performance impairment in children, headaches and fatigue, sleep disorders, neurodegenerative conditions, reduction in melatonin secretion and cancers (BioInitiative Report Chapters 5–10, 12) [1].

This information now argues for thresholds or guidelines that are substantially below current FCC and ICNIPR standards for whole-body exposure. Uncertainty about how low such standards might have to go to be prudent from a public health standpoint should not prevent reasonable efforts to respond to the information at hand. No lower limit for bioeffects and adverse health effects from RF has been established, so the possible health risks of wireless WLAN and WI-FI systems, for example, will require further research and no assertion of safety at any level of wireless exposure (chronic exposure) can be made at this time. The lower limit for reported human health effects has dropped 100-fold below the safety standard (for mobile phones and PDAs); 1000–10,000-fold for other wireless (cell towers at distance; WI-FI and WLAN devices). The entire basis for safety standards is called into question, and it is not unreasonable to question the safety of RF at any level.

A cautionary target level for pulsed RF exposures for ambient wireless that could be applied to RF sources from cell tower antennas, WI-FI, WI-MAX and other similar sources

is proposed. The recommended cautionary target level is 0.1 microwatts per centimeter squared ($\mu W/cm^2$) (or 0.614 V per meter or V/m) for pulsed RF where these exposures affect the general public; this advisory is proportionate to the evidence and in accord with prudent public health policy. A precautionary limit of 0.1 $\mu W/cm^2$ should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. An outdoor precautionary limit of 0.1 $\mu W/cm^2$ would mean an even lower exposure level inside buildings, perhaps as low as 0.01 $\mu W/cm^2$. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

Broadcast facilities that chronically expose nearby residents to elevated RF levels from AM, FM and television antenna transmission are also of public health concern given the potential for very high RF exposures near these facilities (antenna farms). RF levels can be in the 10 s to several 100 s of $\mu W/cm^2$ in residential areas within half a mile of some broadcast sites (for example, Lookout Mountain, Colorado and Awbrey Butte, Bend, Oregon). Like wireless communication facilities, RF emissions from broadcast facilities that are located in, or expose residential populations and schools to elevated levels of RF will very likely need to be re-evaluated for safety.

For emissions from wireless devices (cell phones, personal digital assistant or PDA devices, etc.) there is enough evidence for increased risk of brain tumors and acoustic neuromas now to warrant intervention with respect to their use. Redesign of cell phones and PDAs could prevent direct head and eye exposure, for example, by designing new units so that they work only with a wired headset or on speakerphone mode.

These effects can reasonably be presumed to result in adverse health effects and disease with chronic and uncontrolled exposures, and children may be particularly vulnerable. The young are also largely unable to remove themselves from such environments. Second-hand radiation, like second-hand smoke is an issue of public health concern based on the evidence at hand.

In summary, the following recommendations are made:

- ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky (at levels generally at 2 mG (0.2 μT) and above).
- While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction, It is also recommended for that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant. This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies.
- While it is not realistic to reconstruct all existing electrical distributions systems, in the short-term; steps to reduce exposure from these existing systems need to be initiated and should be encouraged, especially in places where children spend time.
- A precautionary limit of 0.1 $\mu W/cm^2$ (which is also 0.614 V per meter) should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

References

[1] C. Sage, D.O. Carpenter (Eds.), BioInitiative Working Group BioInitiative Report: A Rationale for a Biologically-based Public

Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. http://www.bioinitiative.org.

[2] REFLEX Program. Risk evaluation of potential environmental hazards from low frequency electromagnetic field exposure using sensitive in vitro methods. A project funded by the European Union under the programme Quality of Life and Management of Living Resources, Key Action 4 (2004).

[3] L. Hardell, C. Sage, Biological effect from electromagnetic field exposure and public exposure standards, Biomed. Pharmacother. 62 (2008) 104–109, doi:10.1016/j.bipha.(2007)12.004.

[4] L. Hardell, M. Carlberg, F. Söderqvist, K. Hansson Mild, Meta-analysis of long-term mobile phone use and the association with brain tumours, Int. J. Oncol. 32 (2008) 1097–1103.

[5] P. Kan, S.E. Simonsen, J.L. Lyon, J.R.W. Kestle, Cellular phone use and brain tumor: a meta-analysis, J. Neurooncol. (2007), doi:10.1007/s11060-007-9432-1.

[6] E. Cardis, Interphone Study Memo, International Agency for Cancer Research, October 2008.

[7] S. Sadetzki, A. Chetrit, A. Jarus-Hakak, E. Cardis, Y. Deutch, S. Dvendevani, A. Zultan, I. Novikov, L. Freedman, M. Wolf, Cellular phone use and risk of benign and malignant parotid gland tumors—a nationwide case–control study, Am. J. Epidemiol. (2008), doi:10.1093/aje/kwm325.

[8] A. Lahkola, T. Salminen, J. Raitanen, S. Heinavaara, M.J. Schoemaker, H.C. Christensen, M. Feychting, C. Johansen, L. Klaeboe, S. Lonn, A.J. Swerdlow, T. Tynes, A. Auvinen, Meningioma and mobile phone use—a collaborative case–control study in five North European countries, Int. J. Epidemiol. Adv. Access (August) (2008), doi:10.1093/ije/dyn155.

[9] T. Takebayashi, S. Akiba, Y. Kikuchi, et al., Mobile phone use and acoustic neuroma risk in Japan, Occup. Environ. Med. 63 (2007) 802–807.

[10] D.O. Carpenter, C.L. Sage, Setting prudent public health policy for electromagnetic field exposures, Rev. Environ. Health 23 (2) (2008) 91–117.

[11] D.O. Carpenter, C.L. Sage, BioInitiative Working Group, Key scientific evidence and public health policy options, BioInitiative Report at http://www.bioinitiative.org, 17 (2007).

[12] European Commission, Health and Consumer Protection, Scientific Committee on SCENIHR Report on Emerging and Newly Identified Health Risks—Possible Effects of Electromagnetic Fields (EMF) on Human Health, 2007.

[13] World Health Organization, Extremely Low Frequency Fields Environmental Health Criteria Monograph 238, 2007. http://www.who.int/peh-emf/project/en and http://www.who.int/peh-emf/meetings/elf_emf_workshop_2007/en/index.html.

[14] http://news.cnet.com/Emerging-markets-fuel-cell-phone-growth/2100-1039_3-6159491.html.

[15] http://news.softpedia.com/news/2-14-billion-cell-phone-subscribers-in-2005-2120.shtml.

[16] http://www.ctia.org/media/industry_info/index.cfm/AID/10323.

[17] http://www.nytimes.com/2008/09/20/us/20messaging.html and Members Info. Electronics Industries Alliance Website, November, 2000.;
Members Info, Electronics Industries Alliance Website, November 2000.

[18] L. Hardell, M. Carlberg, K. Hansson Mild, Pooled analysis of two case–control studies on use of cellular and cordless telephones and the risk for malignant brain tumours diagnosed in 1997–2003, Int. Arch. Environ. Health 79 (2006) 630–639, doi:10.1007/s00420-006-0088-5.

[19] M. Kundi, The controversy about a possible relationship between mobile phone use and cancer, Environ. Health Persp. (September) (2008), doi: 101289/ehp.11902.

[20] J. Pronczuk-Garbino (Ed.), Children's Health and the Environment: A Global Perspective, World Health Organization, Geneva, Switzerland, 2005, p. 367.

[21] World Health Organization, Children's Health and Environment: A Review of Evidence: A Joint Report from the European Environmental Agency and The World Health Organization, 2002. http://www.who.int/peh-emf.

[22] O.P. Gandhi, G. Lazzi, C.M. Furse, Electromagnetic absorption in the human head and neck for mobile telephones at 835 and 1900 MHz, IEE Trans. Microw. Theory Tech. 44 (1996) 1884–1896.

[23] O.P. Gandhi, G. Kang, Some present problems and a proposed experimental phantom for SAR compliance testing of cellular telephones at 835 and 1900 MHz, Phys. Med. Biol. 47 (2002) 1501–1518.

[24] J. Wiart, A. Hadjem, M.F. Wong, I. Bloch, Analysis of RF exposure in the head tissues of children and adults, Phys. Med. Biol. 53 (2008) 3681–3695;
J. Wiatt, A. Hadjem, M.F. Wong, I. Bloch, Analysis of RF exposure in the head tissues of children and adults, Wiatt Phys. Med. Biol. 53 (June) (2008) 2771–2783.

[25] H.A. Divan, L. Kheifets, C. Obel, J. Olsen, Prenatal and postnatal exposure to cell phone use and behavioral problems in children, Epidemiology 19 (4) (2008).

[26] International Commission on Non-ionizing Radiation Protection, Guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz). Health Phys. 74(4) (1998) 494–522. http://www.icnirp.de.

[27] Institute of Electrical and Electronics Engineers, Inc (IEEE), Section 4.2 of "IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz," ANSI/IEEE C95.1-1992. New York, NY, 1992.

[28] H. Lai, N.P. Singh, Single and double strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation, Int. J. Radiat. Biol. 69 (1996) 513–521.

[29] S. Ivancsits, A. Pilger, E. Diem, O. Jahn, H.W. Rudinger, Cell type-specific genotoxic effects of intermittent extremely-low frequency electromagnetic fields, Mutat. Res. 583 (2005) 184–188.

[30] J. Phillips, et al., DNA damage in molt-4 lymphoblastoid cells exposed to cellular telephone radiofrequency fields in vitro, Bioelectrochem. Bioenerg. 45 (1998) 103–110.

[31] R.J. Aitken, L.E. Bennetts, D. Sawyer, A.M. Wiklendt, B.V. King, Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline, Int. J. Androl. 28 (2005) 171.

[32] J.Y. Kim, S.Y. Hong, Y.M. Lee, S.A. Yu, W.S. Koh, J.R. Hong, T. Son, S.K. Chang, M. Lee, In vitro assessment of clastogenicity of mobile-phone radiation (835 MHz) using the alkaline comet assay and chromosomal aberration test, Environ. Toxicol. 23 (2008) 319.

[33] S. Lixia, K. Yao, W. Kaijun, I. Deglang, H. Huajun, G. Xiangwei, W. Baohong, Z. Wei, L. Jianling, W. Wei, Effects of 1.8 GHz radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells, Mutat. Res. 602 (2006) 135.

[34] R. Paulraj, J. Behari, Single strand DNA breaks in rat brain cells exposed to microwave radiation, Mutat. Res. 596 (2006) 76.

[35] M. Mashevich, D. Folkman, A. Kesar, A. Barbul, R. Korenstein, E. Jerby, L. Avivi, Exposure of human peripheral blood lymphocytes to electromagnetic fields associated with cellular phones leads to chromosomal instability, Bioelectromagnetics 24 (2003) 82.

[36] I.G. Akoev, M.S. Pashovkina, L.P. Dolgacheva, T.P. Semenova, V.L. Kalmykov, Enzymatic activity of some tissues and blood serum from animals and humans exposed to microwaves and hypothesis on the possible role of free radical processes in the nonlinear effects and modification of emotional behavior of animals, Radiat. Biol. Radioecol. 42 (3) (2002) 32–330.

[37] C. Blackman, et al., The influence of 1.2 μT, 60 Hz magnetic fields on melatonin and tamoxifen-induced inhibition of MCF-7 cell growth, Bioelectromagnetics 22 (2) (2001) 122–128.

[38] D.E. Blask, S.M. Hill, Effects of melatonin on cancer: studies on MCF-7 human breast cancer cells in culture, J. Neural Transm. Suppl. 21 (1986) 433–449.

[39] J.B. Burch, J.S. Reif, C.W. Noonan, T. Ichinose, A.M. Bachand, T.L. Koleber, M.G. Yost, Melatonin metabolite excretion among cellular telephone users, Int. J. Rad. Biol. 78 (2002) 1029–1036.

[40] Girgert, et al., Induction of tamoxifen resistance in breast cancer cells by ELF electromagnetic fields, Biochem. Biophys. Res. Commun. 336 (2005) 1144–1149.

[41] Harland, et al., Environmental magnetic fields inhibit the antiproliferative action of tamoxifen and melatonin in a human breast cancer cell line, Bioelectromagnetics 18 (1997) 555–562.

[42] Harland, et al., Evidence for a slow time-scale of interaction for magnetic fields inhibiting tamoxifen's antiproliferative action in human breast cancer cells, Cell Biochem. Biophys. 31 (3) (1999) 295–306.

[43] A. Ilhan, A. Gurel, F. Armutcu, S. Kamisli, M. Iraz, O. Akyol, S. Ozen, Ginkgo biloba prevents mobile phone-induced oxidative stress in rat brain, Clin. Chim. Acta 340 (1–2) (2004) 153–162.

[44] Ishido, et al., Magnetic fields (MF) of 50 Hz at 1.2 μT as well as 100 μT cause uncoupling of inhibitory pathways of adenylyl cyclase mediated by melatonin 1a receptor in MF-sensitive MCF-7 cells, Carcinogenesis 22 (7) (2001) 1043–1048.

[45] H. Koylu, H. Mollaoglu, F.N. Ozguner, Melatonin modulates 900 Mhz microwave-induced lipid peroxidation changes in rat brain, Toxicol. Ind. Health 22 (5) (2006) 211–216.

[46] R.P. Liburdy, T.R. Sloma, et al., ELF magnetic fields, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER+ breast cancer cell proliferation, J. Pineal Res. 14 (1993) 89–97.

[47] R.P. Liburdy, et al., Magnetic Fields, melatonin, tamoxifen and human breast cancer cell growth, in: R.G. Stevens, B.W. Wilson, L.E. Anderson (Eds.), The Melatonin Hypothesis—Breast Cancer and Use of Electric Power, Battelle Press, Columbus, Richland, 1997, pp. 669–700.

[48] L.I. Loberg, Gene expression in human breast epithelial cells exposed to 60 Hz magnetic fields, Carcinogenesis 20 (1999) 1633–1636.

[49] Luben, et al., Replication of 12 mG EMF effects on melatonin responses of MCF-7 breast cancer cells in vitro, in: Abstract A-1 of the 1996 Annual Review of Research on Biological Effects of Electric and Magnetic Fields from the Generation, Delivery and Use of Electricity, San Antonio, TX, November 17–21, 1996, p. 1.

[50] Luben, et al., Independent replication of 60-Hz 1.2 μT EMF effects on melatonin and tamoxifen responses of MCF-7 cells in vitro, in: Abstract A-3.4, Bioelectromagnetics Society Annual Meeting, St. Pete Beach, FL, June 7–11, 1998, pp. 17–18.

[51] Morris, In vitro exposure of MCF-7 human breast cancer cells to 60-Hz magnetic fields, in: Abstract p-125A, Bioelectromagnetics Society Annual Meeting, St. Pete Beach, FL, June 7–11, 1998, pp. 204–205.

[52] F. Oktem, F. Ozguner, H. Mollaoglu, A. Koyu, E. Uz, Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin, Arch. Med. Res. 36 (4) (2005) 350–355.

[53] F. Ozguner, G. Aydin, H. Mollaoglu, O. Gokalp, A. Koyu, G. Cesur, Prevention of mobile phone induced skin tissue changes by melatonin in rat: an experimental study, Toxicol. Ind. Health 20 (6–10) (2004) 133–139.

[54] F. Ozguner, A. Altinbas, M. Ozaydin, A. Dogan, H. Vural, A.N. Kisioglu, G. Cesur, N.G. Yildirim, Mobile phone-induced myocardial oxidative stress: protection by a novel antioxidant agent caffeic acid phenethyl ester, Toxicol. Ind. Health 21 (9) (2005) 223–230.

[55] A.W. Guy, C.K. Chou, L.L. Kunz, J. Crowley. J. Krupp, Effects of long-term low-level radiofrequency radiation exposure on rats. US Air Force School of Aerospace Medicine Brooks Air Force Base, Texas TR-85-64 Final Report August 1985, Approved for public release: distribution is unlimited.

[56] C.K. Chou, Long-term low level microwave irradiation of rats, Bioelectromagnetics 13 (1992) 469–496.

[57] H. Dolk, et al., Cancer incidence near radio and television transmitters in Great Britain, Am. J. Epidemiol. 145 (1) (1997) 1–9.

[58] V. Garaj-Vrhovac, D. Horvat, Z. Koren, The relationship between colony-forming ability, chromosome aberrations and incidence of micronuclei in V79 Chinese hamster cells exposed to microwave radiation, Mutat. Res. 263 (3) (1991) 143–149.

[59] V. Garaj-Vrhovac, A. Fucic, D. Horvat, The correlation between the frequency of micronuclei and specific chromosome aberrations in human lymphocytes exposed to microwave radiation in vitro, Mutat. Res. 281 (3) (1992) 181–186.

[60] V. Garaj-Vrhovac, Micronucleus assay and lymphocyte mitotic activity in risk assessment of occupational exposure to microwave radiation, Chemosphere 39 (13) (1999) 2301–2312.

[61] M. Ha, H. Im, M. Lee, H.J. Kim, B.C. Kim, Y.M. Gimm, et al., Radio-frequency radiation exposure from AM radio transmitters and childhood leukemia and brain cancer, Am. J. Epidemiol. 166 (2007) 270–279.

[62] B. Hocking, et al., Cancer incidence and mortality and proximity to TV towers, Med. J. Aust. 165 (11–12) (1996) 601–605.

[63] B. Hocking, Decreased survival for childhood leukemia in proximity to TV towers, in: Poster Presented at the Annual Scientific Meeting of the Royal Australian College of Physicians in Adelaide, SA, Australia, May, 2000.

[64] D.E. Foliart, B.H. Pollock, G. Mezei, R. Iriye, J.M. Silva, K.L. Epi, L. Kheifets, M.P. Lind, R. Kavet, Magnetic field exposure and long-term survival among children with leukemia, Brit. J. Cancer 94 (2006) 161–164.

[65] A. Huss, A. Spoerri, M. Egger, Röösli for the Swiss national cohort study, residence near power lines and mortality from neurodegenerative diseases: longitudinal study of the Swiss population, Am. J. Epidemiol. (November) (2008) (Epub ahead of print).

[66] F. Marinelli, D. La Sala, G. Cicciotti, L. Cattini, C. Trimarchi, S. Putti, A. Zamparelli, L. Giuliani, G. Tomassetti, C. Cinti, Exposure to 900 MHz electromagnetic field induces an unbalance between pro-apoptotic and pro-survival signals in T-lymphoblastoid leukemia CCRF-CEM cells, J. Cell Physiol. 198 (2) (2004) 324–332.

[67] P. Michelozzi, C. Ancona, D. Fusco, F. Forastiere, C.A. Perucci, Risk of leukemia and residence near a radio transmitter in Italy, Epidemiology 9 (Suppl.) (1998) 354.

[68] M. Repacholi, et al., Lymphomas in Eμ-Pim1 transgenic mice exposed to pulsed 900 MHz electromagnetic fields, Radiat. Res. 147 (1997) 31–40.

[69] A. Stang, et al., The possible role of radiofrequency radiation in the development of uveal melanoma, Epidemiology 12 (1) (2001) 7–12.

[70] M. Blank (2007). Section 7, pp. 1–40. Evidence for Stress Response (Stress Proteins). In BioInitiative Report: A Scientific Perspective on Health Risk of Electromagnetic Fields. Published Online 31August 2007, http://www.bioinitiative.org/report/index.htm.

[71] C. Daniells, I. Duce, D. Thomas, P. Sewell, J. Tattersall, D. de Pomerai, Transgenic nematodes as biomonitors of microwave-induced stress, Mutat. Res. 399 (1998) 55–64.

[72] D. de Pomerai, et al., Non-thermal heat-shock response to microwaves, Nature 405 (2000) 417–418.

[73] S. Kwee, et al., The biological effects of microwave radiation, in: Proceedings of the Second World Congress for Electricity and Magnetism in Biology and Medicine, Bologna, Italy, June, 1997.

[74] S. Kwee, et al., Changes in cellular protiens due to environmental non-ionizing radiation. I. Heat-shock proteins, Electro Magnetobiol. 20 (2001) 141–152.

[75] D. Leszczynski, S. Oenväärä, J. Reivinen, R. Kuokka, Non-thermal activation of the hsp27/p38MAPK stress pathway by mobile phone radiation in human endothelial cells: molecular mechanism for cancer- and blood–brain barrier-related effects, Differentiation 70 (2002) 120–129.

[76] D. Leszczynski, R. Nylund, S. Joenvaara, J. Reivinen, Applicability of discovery science approach to determine biological effects of mobile phone radiation, Proteomics 4 (2) (2004) 426–431.

[77] S. Lixia, Y. Ke, W. Kaijun, L. Dequiang, H. Huajun, G. Xiangwei, W. Baohong, Z. Wei, L. Jianling, W. Wei, Effects of 1.8 GHz

radiofrequency field on DNA damage and expression of heat shock protein 70 in human lens epithelial cells, Mutat. Res. (2006), doi:10.1016/j.mrfmmm.2006.08.010.

[78] M. Simko, C. Hartwig, M. Lantow, M. Lupke, M.O. Mattsson, Q. Rahman, J. Rollwitz, Hsp 70 expression and free radical release after exposure to non-thermal radiofrequency electromagnetic fields and ultrafine particles in human Mono Mac 6 cells, Toxicol. Lett. 161 (2006) 73–82 (Elsevier Science Direct).

[79] S. Velizarov, The effects of radiofrequency fields on cell proliferation are non-thermal, Bioelectrochem. Bioenerg. 48 (1999) 177–180.

[80] D. Weisbrot, H. Lin, L. Ye, M. Blank, R. Goodman, Effects of mobile phone radiation on reproduction and development in *Drosophila melanogaster*, J. Cell Biochem. 89 (1) (2003) 48–55.

[81] T. Olivares-Banuelos, L. Navarro, A. Gonzalez, R. Drucker-Colin, Differentiation of chromaffin cells elicited by ELF MF modifies gene expression pattern, Cell Biol. Int. 28 (2004) 273–279.

[82] R. Zhao, S. Zhang, Z. Xu, L. Ju, D. Lu, G. Yao, Studying gene expression profile of rat neuron exposed to 1800 MHz radiofrequency electromagnetic fields with cDNA microassay, Toxicology 235 (2007) 167–175.

[83] A. Karinen, S. Heinavaara, R. Nylund, D. Leszczynski, Mobile phone radiation might alter protein expression in human skin, BMC Genomics 9 (2008) 77, doi:10.1186/1471-2164-9-77.

[84] J. Vanderstraeten, L. Verschaeve, Gene and protein expression following exposure to radiofrequency fields from mobile phones, Environ. Health Persp. 116 (2008) 1131–1135.

[85] G. Abdel-Rassoul, O.A. El-Fateh, M.A. Salem, A. Michael, F. Farahat, M. El-Batanouny, E. Salem, Neurobehavioral effects among inhabitants around mobile phone base stations, Neurotoxicology 28 (2007) 434–440.

[86] P. Acherman, Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG, Neuroreport 11 (15) (2000) 3321–3325.

[87] E.S. Altpeter, T.H. Krebs, Study on health effects of the shortwave transmitter station of Schwarzenburg, Bern, Switzerland, University of Bern BEW Publications Study No. 56, The Federal Office of Energy, 1995.

[88] A.A. Borbely, et al., Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram, Neurosci. Lett. 275 (3) (1999) 207–210.

[89] R. Huber, T. Graf, K.A. Cote, L. Wittmann, E. Gallmann, D. Matter, J. Schuderer, N. Kuster, A.A. Borbely, P. Achermann, Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG, Neuroreport 11 (15) (2000) 3321–3325.

[90] K. Mann, Effects of pulsed high-frequency electromagnetic fields on human sleep, Neuropsychobiology 33 (1996) 41–47.

[91] G. Oberfeld, The microwave syndrome—further aspects of a Spanish study, in: Proceedings of the Third International Workshop on Bioelectromagnetic Effects of Electromagnetic Fields, Kos, Greece, 2004.

[92] R. Santini, M. Seigne, L. Bonhomme-Faivre, S. Bouffet, E. Defrasne, M. Sage, Symptoms experienced by users of digital cellular phones: a pilot study in a French engineering school, Pathol. Biol. (Paris) 49 (3) (2001) 222–226.

[93] R. Santini, P. Santini, P. Le Ruz, J.M. Danze, M. Seigne, Survey study of people living in the vicinity of cellular phone base stations, Electromag. Biol. Med. 22 (2003) 41–49.

[94] TNO Physics and Electronics Laboratory, The Netherlands, Effects of Global Communication System Radio-frequency Fields on Well-being and Cognitive Functions of Human Beings With and Without Subjective Complaints, Netherlands Organization for Applied Scientific Research (2003), pp. 1–63.

[95] E.S. Altpeter, T.H. Krebs, Study on health effects of the shortwave transmitter station of Schwarzenburg, Bern, Switzerland, University of Bern BEW Publications Study No. 56, The Federal Office of Energy, Switzerland, 1995.

[96] S.E. Chia, Prevalence of headache among handheld cellular telephone users in Singapore: a community study, Environ. Health Persp. 108 (11) (2000) 1059–1062.

[97] H. Chiang, et al., Health effects of environmental electromagnetic fields, J. Bioelectr. 8 (1989) 127–131.

[98] H. D'Costa, et al., Human brain wave activity during exposure to radiofrequency field emissions from mobile phones, Aust. Phys. Eng. Sci. Med. 26 (4) (2003).

[99] H.P. Hutter, H. Moshammer, P. Wallner, M. Kundi, Subjective symptoms, sleeping problems and cognitive performance in subjects living near mobile phone base stations, Occup. Env. Med. 63 (2006) 307–313.

[100] M. Koivisto, et al., Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans, Neuroreport 11 (2000) 413–415.

[101] M. Koivisto, et al., The effects of electromagnetic field emitted by GSM phones on working memory, Neuroreport 11 (2002) 1641–1643.

[102] A.A. Kolodynski, V.V. Kolodynska, Motor and psychological functions of school children living in the area of the Skrunda radio location station in Latvia, Sci. Total Environ. 180 (1996) 87–93.

[103] C.M. Krause, L. Sillanmaki, M. Koivisto, A. Haggqvist, C. Saarela, A. Revonsuo, M. Laine, H. Hamalainen, Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task, Neuroreport 11 (4) (2000) 761–764.

[104] C.M. Krause, L. Sillanmaki, M. Koivisto, A. Haggqvist, C. Saarela, A. Revonsuo, M. Laine, H. Hamalainen, Effects of electromagnetic fields emitted by cellular phones on the electroencephalogram during a visual working memory task, Int. J. Radiat. Biol. 76 (12) (2000) 1659–1667.

[105] J. Lass, et al., Effects of 7 Hz-modulated 450 MHz electromagnetic radiation on human performance in visual memory tasks, Int. J. Radiat. Biol. 73 (10) (2002) 937–944.

[106] A.A. Marino, E. Nilsen, C. Frilot, Nonlinear changes in brain electrical activity due to cell phone radiation, Bioelectromagnetics 24 (5) (2003) 339–346.

[107] G. Oberfeld, et al., The microwave syndrome—further aspects of a Spanish study, in: Proceedings of the Third International Workshop on Bioelectromagnetic Effects of Electromagnetic Fields, Kos, Greece, 2004.

[108] A. Preece, et al., Effect of a 915-MHz simulated mobile phone signal on c function in man, Int. J. Radiat. Biol. 75 (1999) 447–456.

[109] S.J. Regel, S. Negovetic, M. Roosli, V. Berdinas, J. Schuderer, A. Huss, U. Lott, N. Kuster, P. Achermann, UMTS base station-like exposure, well-being and cognitive performance, Environ. Health Persp. 114 (2006) 1270–1275.

[110] S. Eltiti, D. Wallace, A. Ridgewell, K. Zougkou, R. Russo, F. Sepulveda, D. Mirshekar-Syahkal, P. Rasor, R. Deeble, E. Fox, Does short-term exposure to mobile phone base station signals increase symptoms in individuals who report sensitivity to electromagnetic fields? A double-blind randomized provocation study, Environ. Health Persp. 115 (2007) 1603–1608.

[111] E.F. Pace-Schott, J.A. Hobson, The neurobiology of sleep: genetics, cellular physiology and subcortical networks, Nat. Rev. Neurosci. 3 (2002) 591–605.

[112] J.B. Burch, J.S. Reif, C.W. Noonan, T. Ichinose, A.M. Bachand, T.L. Koleber, M.G. Yost, Melatonin metabolite excretion among cellular telephone users, Int. J. Radiat. Biol. 78 (2002) 1029–1036.

[113] M.L. Clark, J.B. Burch, M.G. Yost, Y. Zhai, A.M. Bachand, C.T. Fitzpatrick, J. Ramaprasad, L.A. Cragin, J.S. Reif, Biomonitoring of estrogen and melatonin metabolites among women residing near radio and television broadcasting transmitters, J. Occup. Environ. Med. 49 (2007) 1149–1156.

[114] L.M. Wang, N.A. Suthana, D. Chaudhury, D.R. Weaver, C.S. Colwell, Melatonin inhibits hippocampal long-term potentiation, Eur. J. Neurosci. 22 (2005) 2231–2237.

[115] M. Ozcan, B. Yilmaz, D.O. Carpenter, Effects of melatonin on synaptic transmission and long term potentiation in two areas of mouse hippocampus, Brain Res. 1111 (2006) 90–94.
[116] R.J. Reiter, L. Tang, J.J. Garcia, A. Munoz-Hoyos, Pharmacological actions of melatonin in oxygen radical pathophysiology, Life Sci. 60 (1997) 2255–2271.
[117] C.W. Noonan, J.S. Reif, J.B. Burch, T.Y. Ichinose, M.G. Yost, K. Magnusson, Relationship between amyloid beta protein and melatonin metabolite in a study of electric utility workers, J. Occup. Environ. Med. 44 (2002) 769–775.
[118] L.G. Salford, A.E. Brun, et al., Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones, Environ. Health Persp. 111 (2003) 881–883.
[119] J.L. Eberhardt, B.R.R. Persson, A.E. Brun, L.G. Salford, L.O.G. Malmgren, Blood–brain barrier permeability and nerve cell damage in rat brain 14 and 28 days after exposure to microwaves from GSM mobile phones, Electromagn. Biol. Med. 27 (2008) 215–229. doi:10.1080_1536370802344037.
[120] L.G. Salford, et al., Permeability of the blood brain barrier induced by 915 MHz electromagnetic radiation continuous wave and modulated at 8, 16, 50 and 200 Hz, Microsc. Res. Tech. 27 (1994) 535–542.
[121] A. Schirmacher, Electromagnetic fields (1.8 GHz) increase the permeability of sucrose of the blood–brain barrier in vitro, Bioelectromagnetics 21 (2000) 338–345.
[122] Y. Hamnerius, Microwave exposure from mobile phones and base stations in Sweden, in: Proceedings of the International Conference on Cell Tower Siting, sponsored by the University of Vienna & Land-Salzburg, Salzburg, Austria, June 7–8, 2000.
[123] E.D. Mantiply, Summary of measured radiofrequency electric and magnetic fields (10 kHz–30 GHz) in the general and work environment, Bioelectromagnetics 18 (1997) 563–577.
[124] Sage Associates, 2004. An Overview of Low-intensity radiofrequency/microwave radiation studies relevant to wireless communications and data, Bioelectromagnetics Society Annual Meeting, Washington DC, June, 2004.
[125] C. Sage, O. Johansson, S.A. Sage, Personal digital assistant (PDA) cell phone units produce elevated extremely-low frequency electromagnetic field emissions, Bioelectromagnetics 28 (7) (2007) 581–582.
[126] C. Sage, O. Johansson, Response to comment on personal digital assistant (PDA) cell phone units produce elevated extremely-low frequency electromagnetic field emissions, Bioelectromagnetics (July) (2007), 17654541.
[127] C. Sage, O. Johansson, Response to comment on measuring ELF fields produced by mobile phones and personal digital assistants (PDAs), Bioelectromagnetics (July) (2007), 17654536.
[128] M. Tuor, S. Ebert, J. Schuderer, N. Kuster, Assessment of ELF magnetic fields from five mobile handsets, in: ITIS Foundation, Conference Presentation, Monte Verita, 2005.
[129] T. Linde, K.H. Mild, Measurement of low frequency magnetic fields from digital cellular telephones, Bioelectromagnetics 18 (1997) 184–186 (Brief communication).
[130] B. Armstrong, G. Theriault, P. Guenel, J. Deadman, M. Goldberg, P. Heroux, Association between exposure to pulsed electromagnetic fields and cancer in electrical utility workers in Ontario and Quebec, Canada, and France 1970–1989, Am. J. Epidemiol. 140 (1994) 805–820.
[131] G.M. Lee, R.R. Neutra, L. Hristova, M. Yost, R.A. Hiatt, A nested case–control study of residential and personal magnetic field measures and miscarriages, Epidemiology 13 (1) (2002) 21–31.
[132] K.D. Li, R. Oudouli, S. Wi, T. Janevic, I. Golditch, T.D. Bracken, R. Senior, R. Rankin, R. Iriye, A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of spontaneous abortion, Epidemiology 13 (2002) 9–20.
[133] G. Theriault, M. Goldberg, A.B. Miller, B. Armstrong, P. Guenel, J. Deadman, E. Imbernon, T. To, A. Chevalier, D. Cyr, C. Wall, Cancer risks associated with occupational exposure to magnetic fields among utility workers in Ontario and Quebec, Canada and France: 1970–1989, Am. J. Epidemiol. 139 (1994) 550–572.
[134] P. Michelozzi, A. Capon, U. Kirchmayer, F. Forastiere, A. Biggeri, A. Barca, C.A. Perucci, Adult and childhood leukemia near a high-power radio station in Rome, Italy, Am. J. Epidemiol. 155 (2002) 1096–1103.
[135] M. Ha, H. Im, M. Lee, H.J. Kim, B.C. Kim, Y.M. Gimm, J.K. Pack, Radio-frequency radiation exposure from AM radio transmitters and childhood leukemia and brain cancer, Am. J. Epidemiol. 166 (2007) 270–279.
[136] C. Sage, D.O. Carpenter (Eds.), BioInitiative Working Group BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF), 2007. www.bioinitiative.org.;
C. Blackman, H. Lai, Chapters 6 and 14 of the BioInitiative Report, 2007.
[137] A. Chiabrera, B. Bianco, E. Moggia, J.J. Kaufman, Bioelectromagnetics 21 (4) (2000) 312–324.
[138] D.J. Panagopoulos, L.H. Margaritis, in: A.C. Harper, R.V. Buress (Eds.), Mobile Telephony Radiation Effects on Living Organisms, 2008, pp. 107–149. ISBN 978:1-60456-436-5.
[139] W.R. Adey, in: P.J. Rosch, M.S. Markov (Eds.), Potential Therapeutic Applications of Nonthermal Electromagnetic Fields: Ensemble Organization of Cells in Tissue as a Factor in Biological Field Sensing, Bioelectromagnetic Medicine, 2004, pp. 1–16.
[140] S. Engstrom, in: P.J. Rosch, M.S. Markov (Eds.), Magnetic Field Generation and Dosimetry, Bioelectromagnetic Medicine, 2004, pp. 39–50.
[141] A. Pilla, in: F.S. Barnes, B. Greenebaum, (Eds.), Mechanisms and Therapeutic Applications of Time-varying and Static Magnetic Fields in Biological and Medical Aspects of Electromagnetic Fields, third edition, 2007, pp. 351–412.
[142] M. Blank, R. Goodman, Initial interactions in electromagnetic field-induced biosynthesis, J. Cell. Physiol. 199 (2004) 359–363.
[143] M. Blank, R. Goodman, A biological guide for electromagnetic safety: the stress response electromagnetic initiation of transcription at specific DNA sites, Bioelectromagnetics 25 (2004) 642–646.
[144] M. Blank, BEMS Soc. Newslett. (January–February) (2008) 6–7.
[145] G. Lotz, Letter from Greg Lotz, PhD, Chief Physical Agents Effects Branch, Division of Biomedical and Behavioral Science, National Institute of Occupational Safety and Health to Richard Tell, Chair, IEEE SCC28 (SC4) Risk Assessment Work Group, June 17, 1999.
[146] P. Grandjean, Implications of the precautionary principle for primary prevention and research, Am. Rev. Public Health 25 (2004) 199–223.
[147] D. Davis, The Secret History of the War on Cancer, Basic Books, 2008.
[148] R. Proctor, Cancer Wars, Harper Collins Publishers, 1995.
[149] European Environmental Agency, Late Lessons from Early Warnings. The Precautionary Principle 1896–2000. Copenhagen, Denmark, 2001.
[150] P. Landrigan, How much do chemicals affect our health? Discover Mag. (2008).
[151] California Air Resources Board, Appendix III Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant. Part B—Health Effects, 2005.

ELSEVIER

Pathophysiology 16 (2009) 247–248

ISP
PATHOPHYSIOLOGY

www.elsevier.com/locate/pathophys

The London Resolution

Olle Johansson *

The Experimental Dermatology Unit, Karolinska Institute, Department of Neuroscience, Stockholm, Sweden

At a scientific conference on 27th November 2007 entitled—"Are Present ICNIRP EMF Exposure Recommendations Adequate?", hosted by Roger Coghill and Robert Verkerk, at the Royal Society, London, scientists endorsed the BioInitiative Report, extended the 2006 Benevento Resolution and resolved that:

"We, the undersigned, do call on the UK Health Protection Agency (HPA), UK Government and all the health protection agencies and governments world-wide, to take note of the findings and recommendations in the Bioinitiative Report (2007) [1] and its predecessors the Benevento Resolution (2006) [2], the Catania Resolution (2002) [3] and the Salzburg Resolution (2000) [4] to immediately reduce the guidelines for exposure to radiofrequency radiation (RF) and extremely low-frequency electromagnetic[1] fields (ELF-EMF) for the following reasons:

- The overwhelming evidence of adverse non-thermal health effects at exposures many times below the current guidelines.
- The near 100% penetration of the market in Europe, the USA and many other markets by mobile phones and increasing penetration elsewhere.
- The vast proliferation of wireless networks and devices beyond those envisaged at the time the current guidelines were set.

We call for the ICNIRP to reconvene as a matter of urgency to reassess the exposure guidelines and to develop and implement biologically based public safety limits reflecting the overall scientific evidence that existing ICNIRP guidelines are not sufficiently protective against health effects from chronic exposures to the rapidly increasing environmental-level ELF-EMF and RF.

Failing that:

- We call for the setting up of an independent body to define new biologically based public exposure limits and/or preventative actions, for ELF-EMF and RF, that address reported biological effects, which, with prolonged exposure, can reasonably be presumed to result in adverse health consequences.
- In the absence of such recommendations we suggest as an intermediate step that the HPA and UK Government immediately implement the ELF-EMF and RF recommendations of the BioInitiative Report 2007 and strive for the recommendations of the Public Health Department of the Government of Salzburg (2002) of 0.06 V/m for outdoor and 0.02 V/m for indoor RF exposure.

Based on the precautionary principle, children and vulnerable groups (such as people with epilepsy and heart conditions) should not be exposed to a risk of harm, thus we propose that

- Children under 16 should use mobile phones and cordless phones for emergency calls only.
- No Wi-fi, WiMax or other forms of wireless networking are placed in homes, schools or public areas or promoted for use thereof.
- That regular and frequent independent audits are undertaken of emissions to ensure that base stations ("masts") do not exceed the new biologically based guidelines at any locality either singly or by accumulation. Such audits should be widely publicised and made available for public scrutiny.

The precautionary principle needs to be implemented."
Signed:

Prof. Christopher Busby, School of Biomedical Sciences, Faculty of Life and Health Sciences, University of Ulsters Coleraine, UK

* Tel.: +46 8 52487073; fax: +46 8 303904.
E-mail address: olle.johansson@ki.se.

[1] Magnetic fields at 50–60 Hz.

0928-4680/$ – see front matter
doi:10.1016/j.pathophys.2009.03.005

Mr. Roger Coghill, MA (Cantab) C Biol Mi Biol MA (Environ Mgt), Coghill Research Laboratories, Pontypool, Wales, UK
Dr. Andrew Goldsworthy, Honorary Lecturer, Imperial College, London, UK
Dr. Lennart Hardell, University Hospital, Orebro University, Orebro, Sweden
Prof. Olle Johansson, Experimental Dermatology Unit, Department of Neuroscience, Karolinska Institute, and The Royal Institute of Technology, Stockholm, Sweden
Dr. Gerd Oberfeld, Public Health Department, Salzburg Government, Salzburg, Austria
Mr. Alasdair Philips, B.Sc. (Eng), Director, Powerwatch, Sutton in the Isle, UK
Mr. Graham Philips, MBCS, Technical Manager, Powerwatch, Ely, UK
Ms Cindy Sage, Co-Editor, BioInitiative Report, Santa Barbara CA, USA
Dr. John Walker, Chartered Physicist, Sutton Coldfield, UK

References

[1] BioInitiative Report, http://www.bioinitiative.org/report/docs/report.pdf.
[2] Benevento Resolution, Electromagnetic Biology and Medicine, 25, 2006, pp. 197–200, http://www.icems.eu/docs/BeneventoResolution.pdf.
[3] Catania Resolution, http://www.plattform-mobilfunk-initiativen.at/englisch/CATANIA_eng.pdf.
[4] Salzburg Resolution, http://www.salzburg.gv.at/salzburg_resolution_e.pdf.

A Pattern of Incompetence and Fraud

Exposing Major Mistakes, Misleading Misrepresentations, and Obvious Omissions in the Arizona Department of Health Services' "Smart" Meter Health Study

Information and Perspective by Warren Woodward
Sedona, Arizona ~ November 2014

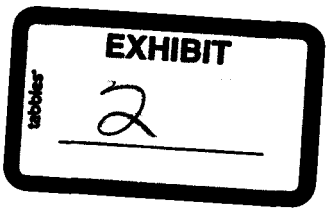


Table of Contents

Foreword ----> Page 2

Introduction – setting goals but not meeting them ----> Page 2

Background – the bamboozle begins ----> Page 3

Radio Frequency Regulations and Literature – the English Muffin Syndrome ----> Page 7

State Studies – what are they doing here? ----> Page 10

Scientific Publication Review – an incredible pattern of fraud becomes obvious ----> Page 18

Individual Health Effects – more wiggling ----> Page 23

Submissions from the (ignored) Community – the deception and fraud continues ----> Page 23

Field Study Follies – more incompetence ----> Page 29

Conclusion – "smart" meters are not found safe ----> Page 33

Full Disclosure: No one is paying me anything to research this issue and ferret out the truth. I received no "dark money". In fact, my work has cost me much of my own money in time and expenses.

Foreword

The title of this report, *A Pattern of Incompetence and Fraud*, was not chosen for affect.

This evaluation of the "smart" meter health study that the Arizona Corporation Commission (ACC) requested of the Office of Environmental Health at the Arizona Department of Health Services (ADHS), will show in detail the multitude of major mistakes, misleading misrepresentations and obvious omissions that comprise the ADHS study. (The ADHS study, *Public Health Evaluation of Radio Frequency Exposure from Electronic Meters,* may be read in its entirety at the ACC docket, here: http://images.edocket.azcc.gov/docketpdf/0000157691.pdf.)

A lover of brevity, I apologize for the length of this report, but the instances of data cherry picking and misrepresentations of scientific studies are too numerous. The spinning and equivocation is endless, the repetition of misinformation seemingly constant. And there are too many examples of ADHS omitting relevant and key material from the scientific works they review.

Then of course there are the simple, basic things that ADHS got completely wrong. As you read, remember that ADHS spent over a year on their study. They had time to get it right but they did not.

As I go through the ADHS study in the order it was written, section by section and sometimes line by line, you will see that an unmistakable pattern emerges, one of incompetence and fraud. The mistakes happen so often that they reflect incompetence, and instances where ADHS misleads occur so often that they amount to willful deception.

In addition to other information, I use the actual articles and studies that ADHS referenced to demonstrate and prove my points. I show what ADHS reported and then what was really said.

The ADHS study is a fraud on the public. Read along with me and you'll see that I am not exaggerating.

Introduction – setting goals but not meeting them

The "Introduction" portion of the ADHS study is fairly uneventful, just standard introductory stuff.

It's worth noting the goals they set forth so you can see later that they failed to meet them.

> "The goals of this report are 1) to determine whether RF exposure from electronic meters on residences, including single family homes and apartment complexes are within the FCC standards or are at levels to cause public health concern; and 2) to determine whether the current body of peer-reviewed literature has found an association between RF exposure from low level RF exposure and adverse health effects."

Notice that an actual investigation of people made ill by "smart" meters was not a goal. That is a major failing and will be discussed in more detail later.

Notice that goal number 2 entails an investigation into peer-reviewed literature. Do you see any goal listed that calls for listing and promoting non-peer-reviewed studies? I don't, yet ADHS saw fit to include six of them from four different states.

ADHS wrote: "ADHS reviewed available peer-reviewed literature to summarize potential health effects from radio frequency exposure, including exposure from electronic meters."

No, ADHS reviewed *some* peer-reviewed literature.

Background – the bamboozle begins

After a primer on electromagnetic fields and radiofrequency [RF] radiation, ADHS tips their hand by inserting this gratuitous bit of industry propaganda: "Electronic meters give utilities a means to match energy consumption with energy generation, and allow consumers to better manage their energy use."

What the heck is that sentence doing in a health report? It sounds like something out of an electric company's bill insert. Not only that but the statement is false.

1. "Electronic meters give utilities a means to match energy consumption with energy generation ...." —> That has been proved wrong by Northeast, Massachusetts' largest electric utility (discussed by me later).

2. "Electronic meters ... allow consumers to better manage their energy use." —> Complete nonsense. Nobody needs a "smart" meter to know when the lights are on. And if for some reason they do, there are energy monitors they can buy that start at $16.

ADHS continues, now with a half truth that is more industry propaganda:

> "Advanced Metering Infrastructure (AMI) meters are devices capable of two-way communication, and use RF frequencies for communication purposes. AMI meters send usage data to the electric company, and the electric companies can communicate with the meter, for example, starting and stopping service remotely."

What is always left unsaid is that wireless "smart" meters also move other people's data, not just yours. Essentially, utilities are taking your property to use for their own communications network. They have put a radio transceiver and relay antenna at your place and not compensated you for it. What if ATT or Verizon did that?

ADHS briefly mentions Power Line Communication (PLC). PLC is another, different method of "smart" meter communication whereby data is sent via existing power lines, not by microwaves.

In what will not be the first time in their study that ADHS shows a complete lack of subject matter knowledge, Table 1 on page 2 of the ADHS study has the PLC frequency listed as 57 – 63 hertz.

The PLC system does *not* transmit at 57 to 63 hertz.

I called the Trico Electric Cooperative in whose territory the Arizona Radiation Regulatory Agency (ARRA) measured for the ADHS study, and I spoke with a technical expert there. Steve Martinez told me Trico uses frequency in the range of 910 to 1122 hertz for its PLC.

ADHS is off by a mile.

Think about that. ADHS had a over a year to get their study right but they got this very basic information completely wrong – information that I was able to get completely right in a very short phone call. How can the rest of what ADHS says have any credibility? What else did they flub? Keep reading; you'll see they flubbed a great deal – and what they didn't flub they misrepresented.

And speaking of misrepresentation, we are now at a point in the ADHS study where the bamboozle of distracting, false comparisons begins.

The electromagnetic spectrum is reproduced on page 3 of the study, and ADHS points out that radio frequency can come "... from natural sources (e.g. the sun) or from man-made sources (e.g. radios)." The study goes on to say, "Some common household items use RF and are regulated by the FCC." To illustrate this point there are pictures of a radio, "smart" meter, microwave oven, television, cell phone and WiFi router, and those are grouped as "Common Household RF Sources".

Comparison with these items is the hallmark of "smart" meter boosters and apologists. A truly objective study of "smart" meter health effects would not include it.

The comparison is designed to create the impression that the "smart" meter is benign. In their propaganda, utilities also use the familiarity of these other items to imply that one more (which happens to be theirs, the "smart" meter) is therefore OK. However, lumping these various items together amounts to an apples and oranges false comparison in several ways.

The items listed – radios, microwave ovens, televisions, cell phones and WiFi routers – are all items one can choose or not choose. For example, by conscious choice I have never owned a microwave oven in my life, and we do not use WiFi in our house but wire our computers instead. I seldom listen to the radio and, when I do, our radio, unlike a "smart" meter, only receives; it does not transmit. Our television does not transmit either. ADHS is completely wrong in listing radios and TVs as "Common Household RF Sources".

Also, if chosen, an individual can limit their usage of the items shown in the ADHS study. For example, I do own a cell phone but my use is so restricted that I do not even know its number. The phone is turned off and kept in my vehicle for emergency purposes. Individuals cannot limit usage of a "smart" meter.

Exposure to "smart" meter radiation is beyond the control of the individual and, in fact, chronic – 24/7/365. Even the sun (which necessitated the invention of the hat for shielding) gives us a break for roughly half the day. The "smart" meter never quits.

Additionally, no one has to pay to "opt out" of the sun. And no one has to pay to "opt out" of a radio, cell phone, TV, microwave, or WiFi router.

False and misleading comparisons continue and abound on page 4 where the ADHS study discusses radio frequency power density, distance from radiation signal, and duration of signal.

From the ADHS: "For example, cell phones and microwave ovens emit radiation at higher power densities than Wi-Fi routers, radios, and smart meters."

Obviously a microwave oven is intentionally heating food but it is not intentional that one be exposed to that radiation which is very high in the oven. Industry typically quotes allowed leakage rates for an oven compared with smart meters. However, the actual typical peak RF from a microwave oven is about 10 microwatts per centimeter squared at one meter away, not much different than a "smart" meter.

As for the cell phone comparison, some cell phones when operating at peak level can produce a signal higher than a smart meter but most operate much lower than a smart meter due to adaptive power control and other measures intended to conserve battery power. No such conservation measures are employed for "smart" meters.

Also, exposure to "smart" meter radiation is whole body exposure whereas exposure to cell phone radiation is generally at the head only. And again, exposure to the devices other than "smart" meters is voluntary and intermittent, not chronic and involuntary as with "smart" meters.

Once again, the ADHS study's authors demonstrate their nearly complete ignorance of the subject by listing radios as RF emitters. Radios are RF receivers. They do not emit RF (unless of course they are a HAM radio).

We encounter an additional faulty comparison in the ADHS example given for distance from a radiation signal:

> "RF exposure decreases rapidly with distance. For the example of microwave ovens, a person 50 cm from a microwave oven receives about 1/100th of the microwave exposure of a person 5 cm away. (WHO 2005)"

Who stands 5 cm (2 inches) from a microwave oven?

With distance, RF does fall off quickly from a source. But a more reasonable, less biased comparison would be standing 3 feet and then moving to 10 feet away from a microwave oven. In that case the RF level *does* drop off, but to about 1/10th the initial value, not 1/100th.

Regarding duration of signal, the study states that "Americans spend on average nearly 3 hours per day on their mobile device per day. (Geekwire 2014) In contrast, smart meters in Arizona typically emit RF less than ½ hour in total during the day."

Several things are wrong with that.

First of all, the Geekwire article is not about how long people spend talking on their cell phones, but rather how long they spend on their "smart" mobile devices while web browsing and using apps.

(http://www.geekwire.com/2014/flurry-report-mobile-phones-162-minutes/)

As if those 3 hours Geekwire mentioned were all phone calls, ADHS has apparently assumed a 100% duty cycle for those 3 hours. In actual fact, it is not really knowable how much of that time involves the transmission of microwaves from the device because, in many of the app/web browsing type uses, the device is primarily receiving incoming data with only intermittent outgoing transmissions to maintain a connection.

In other words, despite ADHS's effort to do so, a definite duty cycle cannot be ascribed to the activity described in the Geekwire article. ADHS has made another meaningless and false comparison.

If anything, the ADHS study should be addressing *why* people who spend "nearly 3 hours per day on their mobile device" are getting sick after chronic exposure to "smart" meter radiation when they weren't getting sick before, especially if that additional radiation totals "less than ½ hour" per day.

The answer would be that "less than ½ hour total during the day" is more like non-stop-all-day when the transmissions are just fractions of seconds in duration. In other words, split second transmissions might add up to less than ½ an hour but, because they are split second transmissions, there are thousands of them continuously during the day and night.

You can see this basically non-stop "smart" meter transmission in my youtube videos **APS Caught Lying Again** and **Navopache Caught Lying**. Can anyone watch those videos and then think that comparison with cell phone use is fair comparison? Has the Dept. of Health Services never heard of the Death of One Thousand Cuts? It's clear from ADHS's false comparison that they do not understand chronic exposure and, in not understanding, did not bother to address or examine it.

By the way, both those videos were sent to ADHS while they were in the process of writing their study, so in my opinion they have no excuses for bungling this important point.

While APS and Navopache Electric continue to lie about the number of their SM transmissions per day (giving ridiculous, low-ball numbers of 125 and 6 respectively), utilities that have been forced to come clean have admitted vastly different numbers – PG&E as many as 190,000 times per day and Sacramento Municipal Utility District (SMUD) as many as 240,396 per day (more than 166 times per minute).

Also, the ADHS statement that "smart meters in Arizona typically emit RF less than ½ hour in total during the day" may not be correct.

Let's say the meters transmit for 1/10 of a second each time. 28 minutes of total transmissions would equal 16,800 transmissions per day. In **APS Caught Lying Again** you can see me measuring a meter I estimate to be transmitting 50,880 times per day. That would total about 1 hour and 20 minutes per day. I'll let you do the math for the far greater PG&E and SMUD numbers.

Lumped in with the study's misleading discussion of radio frequency power density, distance from radiation signal, and duration of signal, is this curious non sequitur: "**RF from the Sun:** Humans can also receive RF radiation from the sun. However, this radiation is at a different frequency from radio waves and microwaves."

As I wrote previously, people have known for thousands of years to shield themselves from the sun's radiation, and the sun is one reason why hats were invented. But how many people know to shield themselves from the radiation of 'smart" meters? Additionally, almost anyone can afford a $10 sun hat but shielding a home from microwaves costs thousands. And personal shielding outside of the home is almost impossible if one wants to live a normal life.

The sun's radiation quits for roughly ½ the day; "smart" meters do not. The sun's rays actually promote life; the "smart" meters' do not. Why is solar radiation even mentioned if not to associate some kind of general beneficence to radiation in the reader's mind? What the heck does solar radiation have to do with the health effects of "smart" meters?

Discussing some "potential health effects from radio frequency" the ADHS study says,

> "This reported sensitivity to EMF has been generally termed "electromagnetic hypersensitivity" or EHS. A survey of occupational medical centers estimated the prevalence of EHS to be a few individuals per million in the population (WHO 2005)."

Actually, the "reported sensitivity to EMF" was named by a German doctor as far back as 1932, and was then more accurately called radio wave sickness.

It is always important to call things what they really are. "Electromagnetic hypersensitivity" connotes that it is the victim's fault for being "hypersensitive" (read "weak"), and not industry's fault for poisoning them.

Also, since exposure to EMF continues to increase exponentially, it is a safe bet that the nine year old survey referenced by ADHS is well out of date. It is also likely that the survey is grossly inaccurate since many doctors are ignorant of the symptoms of radio wave sickness and so misdiagnose and mis-medicate. Indeed, many people have cured their own radio wave sickness, in spite of their doctor's misdiagnosis, by removal of the offending EMF sources, the "smart" meter being one of the major culprits.

Radio Frequency Regulations and Literature – The English Muffin Syndrome

In its discussion of "Radio Frequency Regulations and Literature", ADHS states, "The Federal Communications Commission (FCC) is an independent agency of the United States government that regulates interstate communications by radio, television, wire, satellite, and cable in the US."

What is not mentioned is that the FCC has a huge regulatory conflict of interest in that it sells frequency bandwidth and is currently chaired by a former communications industry lobbyist. This fox/hen house scenario is just one reason the FCC "guidelines" are dangerously lax and out of date (they date to 1996).

The FCC guidelines only involve protection against thermal radiation – when human tissue is heated. British physicist Cyril M. Smith, co-author of the best-seller *Electromagnetic Man*, dubbed this inadequate standard the English Muffin Syndrome – *If it's not burnt, it's all right.*

Additionally, FCC guidelines were based on a test population of average weight males. What about sensitive populations such as children and pregnant women?

Sadly – and negligently – FCC exposure guidelines do not cover non-thermal, low intensity radiation generated by "smart" meters and other wireless devices at the lower end of the microwave range. The FCC exposure guidelines are thus completely inapplicable for the microwave radiation emitted by "smart" meters.

Here are two comprehensive explanations of what I have just stated. Both are written for the layperson.

> *Serious Flaws with the FCC RF/MW Safety Guidelines*
> http://www.emrpolicy.org/faq/fcc_flaws.pdf
>
> *A Primer on FCC Guidelines for the Smart Meter Age*
> http://stopsmartmeters.org/2012/03/09/a-primer-on-the-fcc-guidelines-for-the-smart-meter-age/#skipmath

And here is a report that goes into more scientific detail:

> *Assessment of Radiofrequency Microwave Radiation Emissions from Smart Meters*
> http://sagereports.com/smart-meter-rf/

There are of course other independent reports for anyone who cares to look.

Here is one more thing about the FCC parameters which is quite interesting. For years during the Cold War the Russians bombarded the U.S. embassy in Moscow with microwave radiation, and many of the embassy workers got cancer, more than what would be normal. The bombardment was within the FCC guidelines.

> The clandestine activation of what became called the "Moscow Signal" would mark the beginning of a twenty-three year undetectable assault on the diplomatic staff of more than 1800 representing the US State Department. According to the famous Lilienfeld Report, the embassy staff would be bathing in a constant field of radio waves for about fifty hours per week that measured between 20 and 100 microwatts. These are levels well within the US safety standards today.
>
> It would be another dozen years before the US Government uncovered this covert operation and not until 1976 before the US Embassy staff would finally be informed. But it would be too late for the three ambassadors, who had served in Moscow. All three died of cancer, two of adult leukemia, which is strongly environmentally-linked. It would be too late for the hundreds of other embassy employees, who fell to a variety of cancers, including breast, prostate, brain, lymphoma and leukemia reaching the alarming rate of eight times the expected mortality rate! It would be too late for more than half the staff who suffered chromosome damage from the menacing rays.
>
> ~ Ann Louise, *Accidental Conspiracy* http://www.annlouise.com/articles/338

For a visual graphic on just how inadequate the FCC guidelines are for protecting human health, search YouTube for **Take Back Your Power - Smart Meter Radiation** and watch the 2 & ¾ minute video. (https://www.youtube.com/watch?v=64SIGJnAGeU)

ADHS provides a table of RF exposure limits derived from the very important sounding International Commission on Non-Ionizing Radiation Protection (ICNIRP) and the Institute of Electrical and Electronics Engineers, Inc. (IEEE).

IEEE is an industry promotional organization. Indeed, at their website they describe themselves as "The world's largest professional association for the advancement of technology".

Just because IEEE engineers can measure microwave radiation and tissue temperature with great precision, why is it assumed they know anything at all about the physiology to which they have applied those measurements to create their standards? I would prefer that radiation exposure limits come from an organization more focused on the advancement of health instead of the advancement of technology.

Unfortunately, IEEE is not without scandals. They have lent their name to fake conferences that exist to bilk unwitting participants. Just do an internet search for "fake IEEE conferences".

To further increase revenue, IEEE accepts papers at conferences but there is no real peer review process. Earlier this year the journal, *Nature*, described how IEEE published over 100 papers that were computer generated gibberish "to prove that conferences would accept meaningless papers." (http://www.nature.com/news/publishers-withdraw-more-than-120-gibberish-papers-1.14763)

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) has a report used by many "smart" meter cheerleaders and apologists. In *Exposure to High Frequency Electromagnetic Fields, Biological Effects and Health Consequences*, ICNIRP states,

> "Results of epidemiological studies to date give no consistent or convincing evidence of a causal relation between RF exposure and any adverse health effect. On the other hand, these studies have too many deficiencies to rule out an association."

You've got to love that as a perfect example of equivocation. There is "no consistent or convincing evidence" but at the same time we can't rule it out. Thank goodness people have only two sides of their mouths otherwise they might have thrown in a third diametrically opposed conclusion.

The people who authored ICNIRP's EMF exposure guidelines were unqualified for that task. One-sided, they rejected peer-reviewed studies that showed DNA damage at low exposure levels. You can read about it in this short article, *ICNIRP Guidelines on Genotoxicity,* here: http://microwavenews.com/short-takes-archive/icnirp-guidelines-genotoxicity .

At their website, ICNIRP portrays itself as independent of industry yet according to the Microwave News "A number of industry consultants advise ICNIRP – Leeka Kheifets and David Black come right to mind." (http://microwavenews.com/short-takes-archive/icnirp-elections-matthes-feychting-are-new-leaders)

By the way, scientist-for-hire Leeka Kheifets was at APS's side at the first Arizona Corporation Commission "smart" meter meeting in September of 2011. She gave a power point presentation largely based on the biased and discredited CCST report (which will be discussed later since ADHS made the mistake of including it in their study).

So ask yourself, would you trust your health, your life, to ICNIRP or IEEE? I know I wouldn't. Reminds me too much of "9 out 10 doctors smoke Camels." When money's involved, many people will do or say anything. Or as Dr. John put it so well in *Babylon*, "This is not the land of milk and honey. This is the place where people sell their souls out for money. And you know they do."

ADHS faithfully parroted the ICNIRP, IEEE, FCC line when they wrote the following about "time-averaging". Sadly, ADHS did not have the wits to realize how preposterous a concept it is, how this major flaw condemns the FCC guidelines to absolute irrelevance regarding health effects:

> "The time-averaging concept can be used to determine the levels of exposure. This means that it is acceptable to exceed the recommended limits for short periods of time as long as the average exposure does not exceed the limit."

Actually, what that means is that they are averaging power density over time to make that power seem OK. It's a way to level off peaks in transmission, to make those peaks disappear.

Think about this: If I hit you with a hammer will it feel better if we "time-average" that blow? Would you like to try that? I can show you on paper how, when averaged out over time, you'll hardly feel anything.

On page 5 of their study, ADHS attempts to dismiss non-thermal radiation effects with a 5 sentence statement from the industry agenda driven and discredited IEEE. In so many words, IEEE claims they are aware of non-thermal effects of microwave radiation but those effects are "insufficient to be considered a health hazard". It has already been established that this "professional association for the advancement of technology" is sloppy and money-driven. Why should we assume this time is different, especially when there are plenty of studies that do in fact show non-thermal effects.

There is a table on page 6 of the ADHS study that shows microwave radiation exposure limits in use in the U.S., Canada, Australia, New Zealand, and Russia. ICNIRP and IEEE limits are listed as well. ADHS says that all those countries but Russia base their standards on ICNIRP. Is it any surprise then, that independent Russia – which is outside the corrupting influence of ICNIRP – would have a more stringent standard?

For a full discussion of the corruption of science involved in countries that rely on ICNIRP, read this dissertation by Don Maisch, PhD: *The Procrustean Approach – Setting Exposure Standards for Telecommunications Frequency Electromagnetic Radiation. An examination of the manipulation of telecommunications standards by political, military, and industrial vested interests at the expense of public health protection.* (http://www.emfacts.com/papers/)

State Studies – What are they doing here?

On pages 7 to 10 of the ADHS study we are treated to a review of "smart" meter studies from

California, Texas, Maine and Vermont. None of the studies are peer-reviewed.

Recall that in its introduction to this study, ADHS gave as one of its 2 goals:

> "... 2) to determine whether the current body of peer-reviewed literature has found an association between RF exposure from low level RF exposure and adverse health effects."

Since ADHS gave as their goal a review of peer-reviewed literature, one wonders then, what this *non*-peer-reviewed literature is doing in ADHS's study, especially since those six studies have all been thoroughly debunked as little more than misinformation and industry propaganda.

Even without a background in science and without knowing anything about the California Council on Science and Technology (CCST), it is easy for anyone capable of critical thought to see that the CCST study is a propaganda piece. The document is supposedly about the health aspects of smart meters. Yet several times, after just a few pages in, one finds the prose peppered with propaganda about how the meters will make the grid "clean", "efficient", "reliable", "safe" and etc.

First of all, Massachusetts' largest utility, Northeast, has proved that "*An Advance Metering System is not a "basic technology platform" for grid modernization and is not needed to realize "all of the benefits of grid modernization.*"" [italics in original] Anyone can read their full report along with my letter about same at the ACC docket here:
http://images.edocket.azcc.gov/docketpdf/0000151238.pdf .

Secondly and more importantly, unless for propaganda purposes, why are the alleged benefits of "smart" meters even mentioned in a study that is supposed to be about "smart' meter microwave radiation health issues?

The CCST report is not primary research. Its conclusions are based on cherry picked information. It has every appearance of "science" for a preconceived outcome because contributors to the report whose findings did not support that preconceived outcome – that "smart" meters pose no public health problems – had their solicited submissions removed but they were still listed as contributors!

Here is what rejected contributor Dr. Magda Havas had to say about the CCST and their report:

> January 17, 2011. The California Council on Science and Technology (CCST) released their report on Smart meters "Health Impacts of Radio Frequency from Smart Meters". Click here to download this document.
>
> CCST invited me to submit a written report as part of a *Technical Response Team* in October 2010. Note: CCST did not offer, and I did not request, payment for my report.
>
> In December I was informed that neither my report nor any of the others would be appended to the final document nor would they be made available to anyone.
>
> My submission does not support the final conclusions in the CCST report and I provide it here for anyone interested. For a pdf copy click here.

The CCST is so intellectually dishonest that they still listed Dr. Havas as a contributor to their report even though they rejected her findings. You can see her name listed on page 36 of the CCST report linked above.

Also on page 36 you'll see the names of two others who had their findings rejected but were still listed as contributors – Dr. De-Kun Li, MD, PhD Senior Reproductive and Perinatal Epidemiologist at the Kaiser Foundation Research Institute, and Cindy Sage, MA, Department of Oncology, University Hospital, Orebro, Sweden.

Outcast Dr. Raymond Richard Neutra, MD, CM, MPH, Dr. PH, former Director of the California EMF Program, can be found listed as a contributor on page 44 of the CCST report. And the rejected California Department of Public Health is listed on page 37.

It's always important to "follow the money" and on page 1 of the CCST's 2012 annual report they brag that "CCST also has strong connections to industry through its membership." (http://www.ccst.us/annualreport/2011-12/2011-12AR.pdf)

The CCST also has strong connections to the U.S. Department of Energy (USDOE), the same U.S. Department of Energy that subsidized the "smart" grid to the tune of 4 billion dollars. (https://gigaom.com/2009/11/24/smart-grid-stimulus-demo-award-winners-unveiled/)

Again on the same page of the CCST's 2012 report, the CCST lists Lawrence Berkeley National Laboratory, Lawrence Livermore National Laboratory, and SLAC National Accelerator Laboratory as "Sustaining Institutions". These labs are USDOE labs and so are funded by USDOE. It's a mutual admiration (and funding) society.

The next state study referenced by ADHS, the Public Utility Commission of Texas' (PUCT) "Report on Health and Radiofrequency Electromagnetic Fields from Advanced Meters" was directly funded by the U.S. Department of Energy. On page ii of the PUCT report it says, "This document is work supported by the Department of Energy under award numbers DE-OE0000092 and DE-OE0000180." (http://www.puc.texas.gov/industry/electric/reports/smartmeter/SmartMeter_RF_EMF_Health_12-14-2012.pdf)

Those two grants totaled millions. Does anyone think that the "smart" grid's sugar daddy, USDOE, would fund a report if it thought the report would conclude that "smart" meters made people sick?

By the way, number 1 on PUCT's list of sources is none other than the CCST study. All these pro-"smart" meter studies reference one another as in a mutual admiration society, and repeat each others' lies and misinformation. Unfortunately, now ADHS is another link in the chain of fraud.

Something else all these sorts of studies and reports have in common is that none were done before the installation of "smart" meters. They were all done as after-the-fact damage control. People got sick and complained, so industry and government funded studies to avoid liability, to tell people there's nothing to worry about, and to tell people made sick by the meters that it's all in their heads.

Alan Rivaldo, the PUCT report's author, confessed in his cover letter to the report that "Staff relied heavily" on CCST, Lawrence Berkeley National Laboratory and the Electrical Power Research Institute to reach their conclusions.

The Electric Power Research Institute (EPRI) is an industry advocacy group. EPRI actually call themselves an "industry collaborative", and they have a very long list of member utilities. At their website, EPRI boasts that members "pool their resources to fund research", and that "While most members are electric utilities, many are firms, government agencies, corporations, or public or private entities engaged in some aspect of the generation, delivery or use of electricity."

Given the above, does anyone think that EPRI is qualified to weigh in on a health debate? Does anyone think EPRI would be offering objective, impartial opinions on anything?

As I mentioned before, Lawrence Berkeley National Laboratory (LBNL) is a USDOE lab and full fledged "smart grid" cheerleader. I've seen their papers and power points on the subject. They love the "smart" meters they are paid to love and are not impartial.

With these three then – CCST, EPRI, and LBNL – as the sources that the PUCT staff "relied heavily on", does anyone think the PUCT report would be objective?

If you answered NO you answered correctly because it was not objective.

In testimony to the Massachusetts Department of Public Utilities, telecommunications standards expert Dr. Don Maisch summed up the PUCT report thus:

> "The report, written for the Public Utilities Commission of Texas (PUCT), was prepared by Alan Rivaldo, a Cyber Security Analyst at PUCT. Titled **Health and RF EMF from Advanced Meters** the report takes the extreme view that a scientific consensus has been reached within the body of scientific evidence for RF, and people who do not understand this are suffering from misconceptions based on faulty assumptions. This supposed consensus according to Rivaldo is that there are no known non-thermal effects from exposure to RF. He asserts that reports of EHS are unrelated to RF exposure but may be due to psychiatric conditions or stress from worry, going on to say that 'scientific studies show that people who are ill are highly receptive to negative suggestions and may demonstrate a nocebo response as a result of these suggestions'. The overall impression given by the report is that the 'weight of scientific evidence', as presented by organizations such as the IEEE, ICNIRP, the FCC and others, is a body of credible research which is above serious reproach. Any claims otherwise come from notorious, biased researchers who lack scientific rigor. In what is unusual for a supposedly scientific document, the report resorts to making personal attacks on a number of people. While serving up a diatribe against anyone claiming that non-thermal effects exist, especially about smart meters, the author altogether overlooks the significant industry biases and level of scientific uncertainty that exists in the RF controversy, relying exclusively on industry sources for his claims. As such, the PUCT report reads more like the writings of a product defence PR company than a scientific review, which it is not." [Maisch's full testimony is here:

http://skyvisionsolutions.files.wordpress.com/2014/05/maisch-submittal-to-the-ma-dpu-on-electric-grid-modernization.pdf]

ADHS boils down the PUCT report to 3 main points. Lifted straight from the PUCT report's executive summary, point number 1 is that:

> "Decades of scientific research have not provided any proven or unambiguous biological effects from exposure to low-level radio frequency signals. All available material was reviewed, and no credible evidence to suggest that smart meters emit harmful amount of EMF radiation was found."

That's important and authoritative sounding but is really total nonsense.

It is always essential to pay attention to the actual words used. "No credible evidence" begs the question, *credible to whom?*

It's not overly surprising that mountains of evidence of biological effects would not be "credible" to author Rivaldo since he has no technical expertise in the subject of health. He was a former Xerox employee and calls himself a cyber-security analyst.

"No credible evidence" is a phrase common to "smart" meter cheerleaders. Here are some other commonly used wiggle words to be on the lookout for when reading studies such as the ones listed by ADHS – and when reading ADHS's own study as well. Dr. Magda Havas says, "These are words used to mislead, downplay, divert from the real meaning intended in scientific studies." And here is her list of wiggle words [red and italics and bold in original]:

1. ***authoritative*** *reviews*: groups who think like us
2. *no* ***clear*** *evidence of adverse health effects*: there is evidence of adverse health effects
3. *while there are* ***small*** *physiological effects*: there are physiological effects
4. *no* ***definite*** *adverse health effects:* there are adverse health effects
5. *need for further research*: delay tactic
   There is always a need for more research to better understand something. The real question is do we have enough of an understanding to change policy?
6. ***possible*** *associations between RF fields and adverse health outcomes*: there are associations between RF fields and adverse health outcomes

Actually there is a boatload of "credible evidence". A primary source would have been Texans made sick by "smart" meters. But as with the ADHS study and the other state studies that ADHS reviewed, the human element is always left out. I'll have more to say about ADHS' mishandling of this

crucial point later in this report.

ADHS' major point number 2 gleaned from the PUCT report is "Smart meters do not emit or utilize ionizing radiation."

I am amazed that is listed as a major takeaway since I don't think anyone in Arizona (or probably Texas either) has made that allegation. The point is a non-sequitur.

Point number 3, again lifted from the report's executive summary (but at least this time credited), is "Smart meters are not intended for, are not designed to, and do not have the capability to harm an individual or direct a person's thoughts or actions (Rivaldo 2012)."

More nonsense. While "smart" meters may not be "designed" or "intended" to cause harm, they *do* in fact have the capability to harm an individual because individuals have been harmed! That was one of the main reasons why the PUCT report was done.

As I mentioned previously, it is outside ADHS' stated goal to include these non-peer-reviewed studies from the four states, but one must *really* question ADHS' judgment for having included the Maine study.

I was able to get the internal emails of the people involved in putting that study together – the "Maine CDC Smart Meters Team". They were completely at sea. They had little idea what they doing. Basics such as how often and when the meters transmitted were completely unknown to them.

For just one example, "Team" member Jay Hyland, sounding very important as the "Director" of the "Maine Radiation Control Program", had this to say *after* the report went out:

> "We are still getting a number of calls per day on the smart meters, AMI, project. There is a fair amount of confusion regarding when the meters broadcast, and what the different pieces of the system are expected to do. My understanding is the meters broadcast on some regular time table like once per hour, unless the meters are acting as a repeater for other meters, in which case the first meter would broadcast 6 times per hour, or something of that nature. Could you please let us know what protocol the meters broadcast under? Answering the when, where, why of the broadcast parameters. Is the maximum broadcast amount something like a tenth of a second every second? The statements we have been hearing and reading say things like "they will be operating for 41 minutes a day" and "they will do most of their communicating at night". While we don't know specifically where this comes from it would be good to know what the protocol or specifications are, because they operate 10% of the time, could easily fall into either of the above statements."

Can everyone agree that "protocol or specifications" would have been "good to know" ***before*** Maine CDC wrote and submitted their report? Wouldn't that have been a basic first step, especially for the Team's "radiation expert"?

Other embarrassing email excerpts and examples of incompetence on the part of the "Maine CDC Smart Meters Team" can be found in my ACC docket submission on the subject. The "Team" was

so lost and out of it they would be comedy if lives were not at stake.

My ACC docket submission also includes all their internal emails which were posted at the Maine Public Utilities Commission docket by the law firm of Taylor, McCormack & Frame. (my ACC docket submission here: http://images.edocket.azcc.gov/docketpdf/0000146483.pdf)

Unfortunately for Arizonans, the uncritical repetition of Maine's sloppy nonsense by ADHS is reminiscent of the gibberish papers accepted and published by the IEEE that I mentioned previously.

One of the points in the Maine report that ADHS chose to pass along was

> "With regards to electromagnetic hypersensitivity (EHS), the smart meters team concluded that the majority of studies indicate that EHS individuals cannot detect EMF exposure any more accurately than non-EHS individuals, and that well controlled and conducted double-blind studies have shown that symptoms were not correlated with EMF exposure."

Wiggle words alert! "Majority of studies" means that there are in fact studies that show the opposite.

Industry has the money to pump out study after study. They have the influence to taint and corrupt government studies as well. Therefore, people doing real, independent research will most likely be in the minority. The intent behind phrases such as "majority of studies" is to create doubt surrounding studies that are in the minority and to marginalize them.

"Weighing the evidence" or "weight of evidence" are similar phrases designed to manipulate perception. Like "majority of studies", it usually means adding up how many studies or evidence is on one side and how much is on the other.

That said, those 'majority of EHS studies' are nonsense when you know how they are conducted. People are expected to react to an RF source like someone would to a light being turned on and off. "Can you feel it now?" "How about now?" While some people *can* react instantaneously to RF, many get sick and stay sick in a way comparable to hay fever. Just because the irritating pollen is removed does not mean they recover immediately.

Shame on ADHS for perpetuating an attempt to marginalize sick people.

ADHS wasted paper to also include the fact that 3 years after the "Team's" report, the Office of the Maine Public Advocate hired True North Associates to measure "smart" meters at 3 residences.

Wow, what an exhaustive, comprehensive sampling! Not surprisingly, True North found the 3 in FCC compliance. Because the FCC guidelines are only thermal based, what that means is that the people who live in those homes can safely rule out being burned by the microwaves they are being bombarded with. I'm sure they are relieved to know that.

ADHS referenced two Vermont studies.

The independent, non-profit EMR Policy Institute did a thorough debunking of the Vermont Department of Health's (VDH) report, "Radio Frequency Radiation and Health: Smart Meters," the first Vermont report reviewed by ADHS. (http://publicservice.vermont.gov/sites/psd/files/Topics/Electric/Smart_Grid/radio_frequency_radiation_and_health_smart_meters%5B1%5D.pdf)

Among its conclusions the EMR Policy Institute found that:

- **"Non-thermal effects are NOT theoretical and HAVE been recognized by experts as problematic."** [**bold** and caps in original]

- "While no reference list is found in VDH's Report, it appears to ignore the wealth of peer-reviewed scientific literature that demonstrates adverse biological effects at exposure levels well below the US FCC RF exposure guidelines."

- "VDH's Report ignores the analysis of the 2008 NAS [National Academy of Sciences] Report that delineates the flawed scientific record upon which FCC's RF safety guidelines are based. Instead VDH finds that "current regulatory standards for RFR from smart meters are sufficient to protect public health.""

- "VDH's Report did not carry out an in-depth analysis to determine if its reliance on the current US FCC RF radiation exposure limits based on science published prior to 1986 fulfills VDH's stated first priority to "focus on prevention, which is perhaps the best investment that can be made in health.""
  (http://www.emrpolicy.org/files/14mar2012_emrpi_VDH_open_letter_SM_Report.pdf)

The EMR Policy institute also criticized VDH for relying on the discredited CCST report.

The EMR Policy Institute hammered VDH so effectively for the faulty methodology and incorrect measuring equipment that VDH used, that I suspect that's the reason Vermont did a second study, this one commissioned by the Vermont Department of Public Safety and titled "An Evaluation of Radio Frequency Fields Produced by Smart Meters Deployed in Vermont" and performed by Richard Tell Associates. (http://publicservice.vermont.gov/sites/psd/files/Topics/Electric/Smart_Grid/Vermont_DPS_Smart_Meter_Measurement_Report_-_Final.pdf)

That is the other flawed Vermont study ADHS chose to include and use to point out that "smart" meters transmit within FCC guidelines (so that, like Vermonters, we can all stop worrying about being burned by "smart" meter microwaves).

Richard Tell's report is obviously another propaganda piece. It contains all the false, meaningless comparisons with other wireless sources that we've seen in other reports. Towards the end it is hard to keep track of how often Tell has mentioned and compared "smart" meter microwave transmissions to that of things like microwave ovens, cordless phones, wireless routers and even big radar installations. Such comparisons are totally off-subject nonsense and have no business being in a supposedly scientific report on "smart" meter microwave transmissions.

Indeed, in his introductory summary Tell wrote, "This study was aimed at assessing compliance of smart meter signal intensities with regulations established by the Federal Communications Commission (FCC) that prescribe limits for safe exposure of humans." So what does that have to do with a microwave oven or a cordless phone?

Tell was following the script of other reports, trying to use familiarity with other microwave emitting products to make "smart" meters seem OK. He was trying to make it seem like it's OK for utilities to bombard us with microwaves because some of us are likely doing it to ourselves anyway. 'Hey, what's a little more amongst friends?' Only it's really a lot more, and we aren't friends.

Tell discredited himself and exposed himself as an industry shill with the inclusion of this off-subject propaganda and lame attempt at perception manipulation. Additionally, at his bio at his website we find out Tell is basically trained in physics, math and radiation sciences. His expertise is not health or epidemiology yet he implied many health claims throughout his report, all of which are based on "compliance" with FCC rules which – guess what? – he helped write!

From his website bio (http://www.radhaz.com/company/richard-tell-bio):

> *During his tenure at the EPA, his program provided technical support to the Federal Communications Commission (FCC) as the FCC adopted new rules for human exposure to RF fields.*

What a sweet deal! Tell can help write guidelines in the public sector and then make a living in the private sector showing how toxic microwave emissions are OK because they fall within those guidelines.

In his report Tell kept mentioning how the FCC guidelines are based on 30 minute exposure time spans. Hello? How about 24/7/365 time spans, which is the real world?

On page 27 Tell described the FCC guidelines thus: "...present day RF exposure limits are based on time-averaged values of RF power densities...."

We are back to my time-averaged hammer blow analogy. Does anyone think Tell would volunteer to get hit with one? After all, if we time average it, it shouldn't have any "adverse health effects".

For Tell to harp on the fact that the meters he measured comply with the inadequate FCC guidelines that he helped write is meaningless in any serious health discussion.

Scientific Publication Review – an incredible pattern of fraud becomes obvious

In the ADHS' "Scientific Publication Review" portion of their study, wiggle words abound as well some outright cherry picking of information, misrepresentation and what looks like deliberate deception.

Here are some wiggle words and phrases from that portion of the study. The crafted language sets

up a slippery slope, and at the bottom lies our ill health.

"the literature is not clear" —> **Remember wiggle word #2?** ***no clear evidence of adverse health effects*** **means that there** ***is*** **evidence of adverse health effects.**

"Other studies concluded exposure to RF from a variety of sources was associated with adverse health outcomes. However, ..." —> **The studies that show harm are always downplayed with a "however" or some other qualifier.**

"Sometimes a study that suggests an exposure is associated with an adverse health outcome is countered by another similar study that suggests there is no adverse health outcome at that exposure level." —> **How often is "sometimes", and isn't that a reason to at least err on the side of caution anyway?**

"In addition, many of these conclusions were based on results that showed biologic changes. Biologic changes do not always lead to the expected adverse health outcome." —> **So if biologic changes don't "always" make people sick then we don't need to worry?**

The slope is getting steeper by the way, as we now get schooled by none other than NASA in the difference between "biological effects" and "adverse health effects".

According to NASA, "Biological effects are alterations of the structure, metabolism, or functions of a whole organism, its organs, tissues, and cells."

But not to worry, because NASA says, "Biological effects can occur without harming health and can be beneficial." —> **Great! Can I get some beneficial cellular alterations from a "smart" meter?**

According to NASA, an "adverse health effect" is "A biological effect characterized by a harmful change in health."

This whole lead-in is to make a lot of room in your mind for ignoring what is really happening, and to prepare you for the rock bottom of the slope in which ill health gets redefined as health. Check out this next paragraph from the ADHS study:

> "For example Juutilainen, et. al. reviewed *in vitro, in vivo,* and human studies on a variety of adverse health outcomes. The authors stated, "the studies discussed in this review indicate that there may be specific effects from amplitude-modulated RF electromagnetic fields on the human central nervous system. The effects reported (changes in EEG, cerebral blood flow and performance in a memory test) are relatively minor, and do not at present allow conclusions concerning possible adverse health effects."

So, breaking that paragraph down, we learn:

- "adverse health outcomes" from microwaves were studied.
- There "may be specific effects" on your "central nervous system".

- Even though there "may be specific effects" it turns out that actual *reported effects* were changes in the electrical activity of your brain (EEG), the blood flow in your brain, and your memory.

- But you do not have to worry because the effects to your brain are "relatively minor" (relative to what?), and "do not at present allow conclusions concerning possible adverse health effects."

Welcome to rock bottom, everyone, where the effects to your memory are so "relatively minor" that you won't even remember them.

It is simply incredible that this deceptive double talk passes for health science, and that it could be repeated in a health study supposedly done for the benefit for Arizonans.

The ADHS "study" gets worse as one reads along. Permit me to translate.

"No consistent evidence has been found ...." **—> So evidence *was* in fact found.**

"They also stated that although there were some studies that suggested adverse outcomes from lower level exposure to RF, this apparent association might be due to many factors including poor study design, errors, or incorrect assumptions regarding exposure conditions." —> **Or maybe, just maybe, these "adverse outcomes" happened because the studies were done right and microwaves really do make people sick, or rather, experience "adverse outcomes."**

"the weight of scientific evidence from 45 peer reviewed investigations" **—> There's that scale again.**

"They concluded that, based on the available information, an elevated cancer risk associated with cell phone use cannot be ruled out because increased cancer risks were observed in epidemiological studies. Yet, all studies have some methodological deficiencies ...." **—> Cancer cannot be ruled out but don't worry because every study has something wrong with it.**

"Overall, this review concluded that: the large majority of individuals who claim to be able to detect low level of radio frequency EMF are not able to do so under double-blind conditions." **—> Just in case you forgot this phony assertion that ADHS picked out of the sloppy Maine study, here it is again.**

"In another study, Karaca et. al. (2012) stated that "the results of our study support the proposition that cell phones may have a potential to cause hazardous effects on the genome; however, in in vivo conditions, the duration of exposure and the capacity of DNA repair may prevent the development of cancer to an extent." **—> You gotta love that one. Cell phones can mess with your genomes but you'll probably get over it, "to an extent."**

Actually, ADHS cherry picked that last sentence, probably because it was one they could find with the qualifying "however". The gist of Emin Karaca's investigation, "The genotoxic effect of radiofrequency on mouse brain," is really quite different than how ADHS is spinning it by representing the entire study with just that one particular sentence.

(http://www.avaate.org/IMG/pdf/Kanaca_et_al_2011.pdf)

Here is a more representative sentence. In discussing his findings, Karaca wrote: "DNA damage has been found to be increased by 10 times compared to the control cell cultures which were not exposed to RF waves."

Karaca then discussed some other studies that showed DNA damage and he concluded, "Therefore, the results of our study support the findings of those previous studies."

And in the study's abstract we find this summary sentence, "Cell phones which spread RF may damage DNA and change gene expression in brain cells."

ADHS should really be ashamed for misrepresenting the Karaca study, and for attempting to mislead Arizonans.

But if you think that's bad, we now come to the part of the ADHS study where some *serious* misleading, misrepresentation and cherry picking of information occurs. As well, the review it's picked from is so bad to begin with that one could almost say it's cherry picking of *mis*-information.

On page 13 of the ADHS study, there is a table that ADHS describes thus: "Vigjayalaxmi compiled the conclusions on the biological effects of RF exposures from various national and international expert groups. Below is a summary table of these conclusions (2014)."

Wow, "national and international expert groups"! Sounds important ..... until you actually read the review. (Here: http://www.mdpi.com/1660-4601/11/9/9376/htm)

It's junk. I knew that as soon as I read this in the introduction:

> "For human health risk assessment, it is essential to use the "weight of scientific evidence" based on the quality of published studies which should include detailed description of RF dosimetry, exposure conditions and protocols consistent with good laboratory practices, sample sizes with sufficient statistical power, as well as confirmation and replication studies conducted by independent researchers. International organizations, such as the Institute of Electrical and Electronic Engineers (IEEE) and the International Commission on Non-Ionizing Radiation Protection (ICNIRP) have considered all of the available peer-reviewed scientific literature and used the weight of scientific evidence approach to set-up the guidelines or standards for RF exposures in occupationally exposed individuals and the general public to protect against established adverse effects [12–14]."

There's that "Weight of the evidence" again, and this time IEEE and ICNIRP have their thumbs on the scale.

But it gets much worse.

I couldn't believe my eyes when I read this on page 24 of Vigjayalaxmi's report:

> "Some "negative" comments. (i) The selection procedure used to select the members in expert groups (EGs) in various countries was neither clear nor transparent. (ii) It was difficult and almost impossible to verify "no conflict of interest" of the members in the EGs. (iii) The criteria used for evaluations were not sufficiently described in some reports. (iv) Some members participated in more than one expert group (for example, the experts in SSI report were also some members of ICNIRP). (v) Several EGs did not consider the health risks associated with mobile phone base stations. (vi) There was an apparent "bias" in selecting the papers for evaluation: the reports that support their analysis were reviewed and left out those that contradict their conclusions."

Why would anyone take this review seriously? Indeed, three "expert group" members had this to say, "There should be some concern that there are working group members who are the very researchers assessing the quality of their own studies."

Not only did ADHS conveniently leave that information out of their study, they also left out the Vigjayalaxmi review's discussion of radiofrequency radiation being classified as a Class 2B carcinogen by the World Health Organization (WHO). In fact, *nowhere* in the ADHS study is the WHO's classification ever discussed or even mentioned.

It's an incredible omission.

ADHS completely left the WHO out of the table they created on page 13 of their study.

The Vigjayalaxmi review actually had two tables in it with more information in each than what ADHS displayed in theirs. ADHS's table is a combination of those two tables and a condensation of the information. *But*, when the tables were combined by ADHS, ADHS omitted the WHO along with the WHO's conclusion that radiofrequency is a Class 2B carcinogen.

Was this omission was another flub by incompetents, or a deliberate attempt to deceive the public? While you are deciding, don't forget that ADHS had over a year to get their study right.

Last in the ADHS's "Scientific Publication Review" section of their study, we come to their discussion of a report by Dr. David Carpenter, MD. Carpenter is an expert in radiofrequency health and he advocates against "smart" meters. Carpenter does not equivocate.

I am guessing ADHS included Carpenter to appear "balanced".

In the paragraph summarizing one of Carpenter's articles, ADHS wrote,

> "Excessive exposure to RF radiation increases risk of cancer, male infertility, and neurobehavioral abnormalities. Smart meters usually produce atypical, relatively potent, and short-pulsed RF microwaves whose biological effects have never been fully tested and may, in fact, be more hazardous than other waveforms. Electronic meters can add significantly to aggregate RF exposure."

In "gotcha" fashion, ADHS then dismisses Carpenter out of hand by saying that the measurements he gave for "smart" meters fall within FCC guidelines, the implication being there

cannot possibly be a problem if measurements fall within FCC guidelines so there is no point in considering Carpenter's findings.

ADHS:

> "However, at further study of the article, the article states that a typical electronic meter with a 5% duty cycle at a distance of **20** cm (= 0.656 ft) emits **11** pW/cm2 of RF radiation. This is equal to **0.11** W/m2, which is well below the FCC community guideline of 6 W/m2."

ADHS doesn't seem to realize or acknowledge that this value is actually just *above* the Russian standard that they discuss later.

Individual Health Effects – more wiggling

In the "Individual Health Effects" portion of the ADHS study, ADHS claims to have "conducted a literature search of peer-reviewed articles on the potential effects of RF radiation." But then ADHS says, "Most of the studies concluded that there was no association between RF exposure at low levels and adverse health outcomes."

"Most of the studies" is a variation on "weight of the evidence". If you entered a room full of snakes and "most" of them were nonvenomous would you feel safe?

Submissions from the (ignored) Community – the deception and fraud continues

In the "Submissions from the Community" portion of the ADHS study, ADHS says, "Arizona residents have submitted a plethora of information to the Arizona Corporation Commission's eDocket relating to RF exposures from electronic meters."

What a pity for Arizonans that ADHS learned nothing from that "plethora".

What a pity for Arizonans that once again ADHS cherry picked that information for inclusion in the ADHS study.

What a pity for Arizonans that, in at least one instance, it is obvious that ADHS had absolutely no understanding of what they were reading, that they were in way over their heads.

ADHS wrote:

> "The types of information submitted by residents included news articles, websites, peer-reviewed studies, documents released by governmental regulatory or advisory bodies, anecdotal descriptions of how residents believed electronic meters were affecting their health, and personal opinions."

So how did ADHS respond to all that information? "ADHS reviewed the peer-reviewed studies and government documents" and ignored the rest.

ADHS claims to have "reviewed all 38 journal articles assessing health implications that were submitted to the ACC's eDocket. ADHS provided a summary and response to the three articles that were most often mentioned articles in Appendix B."

Why only the top three? Who knows? Perhaps it was so ADHS did not have to deal with other studies that they didn't think they could spin.

At Appendix B, ADHS reviewed those top three starting with "Electromagnetic and Radiofrequency Fields Effect on Human Health" by The American Academy of Environmental Medicine (AAEM). ADHS listed that article's salient points as:

- In the last 20 years, physicians began seeing patients who reported that electric power lines, televisions, and other electrical devices caused a wide variety of symptoms.

- Multiple studies correlate RF exposure with diseases such as cancer, neurological disease, reproductive disorders, immune dysfunction, and electromagnetic hypersensitivity.

- Exposure limits determined by the FCC and other regulatory agencies do not account for effects from non-thermal radiation.

Still cherry picking, ADHS saw fit not to include what the AAEM itself listed as the salient points of its own statement:

- An immediate caution on Smart Meter installation due to potentially harmful RF exposure.

- Accommodation for health considerations regarding EMF and RF exposure, including exposure to wireless Smart Meter technology.

- Independent studies to further understand the health effects from EMF and RF exposure.

- Recognition that electromagnetic hypersensitivity is a growing problem worldwide.

- Understanding and control of this electrical environmental bombardment for the protection of society.

- Consideration and independent research regarding the quantum effects of EMF and RF on human health.

- Use of safer technology, including for Smart Meters, such as hard-wiring, fiber optics or other non-harmful methods of data transmission.

(http://www.aaemonline.org/emf_rf_position.html)

ADHS completely dismissed the AAEM findings by simply saying, "AAEM are not recognized by the American Board of Medical Specialties."

I guess *that* settles *that* then doesn't it? No point in listening to *that* organization. It didn't join the trade association. And never mind that most of the individual members of AAEM *are* members of the American Board of Medical Specialties.

From the AAEM website (http://www.aaemonline.org/):

> "AAEM physicians have earned a recognized MD or DO degree by an accredited medical school in the United States, Canada or other countries and maintain current licensure to practice medicine. Most AAEM physician members are board certified by one or more of the 24 medical specialty boards of the American Board of Medical Specialties."

Also from the AAEM website:

> "The mission of the American Academy of Environmental Medicine is to promote optimal health through prevention, and safe and effective treatment of the causes of illness by supporting physicians and other professionals in serving the public through education about the interaction between humans and their environment."

Isn't that what the Office of Environmental Health at ADHS should be doing instead of kissing off an organization that really *does* do that?

The AAEM is:

> **The Academy of Firsts:** The founders and members of the American Academy of Environmental Medicine are recognized as the first to describe or the first organization to acknowledge ...

- Serial Dilution Endpoint Titration
- Sublingual Immunotherapy
- Optimal Dose Immunotherapy
- Food Allergy/Addiction
- Provocation/Neutralization
- Avoidance/Reintroduction Challenge Testing
- Rotary Diversified Diet
- Chemical Sensitivity (MCS)
- Total Load Phenomenon
- Environmental Control in the Home, Workplace, and Hospital
- Chemically Less-Contaminated Foods
- Sauna Depuration
- Hepatic Detoxication Enhancement
- Gulf War Syndrome
- Endocrine Mimicry Disorders

- The Role of Mold in the Development of Systemic Illness
- Yeast Syndrome
- CFID/FMS

But never mind all that. Never mind that these are board certified doctors who have made studying the effect of environment on health a priority. Never mind that most of them as individuals are certified by the American Board of Medical Specialties. If their organization as a whole is not part of that certain trade group then forget it, ADHS will not even consider them. What arrogance!

Another article ADHS reviewed in Appendix B is "Update and Review of Research on Radiofrequencies: Implications for a Prudent Avoidance Policy in Toronto" by Loren Vanderlinden (*not* Vanderlin as reported by ADHS) for the Environmental Protection Office at Toronto Public Health (TPH). (http://www.healthyenvironmentforkids.ca/sites/healthyenvironmentforkids.ca/files/epche-resources/TPH_RFtechnical_report.pdf)

As usual, ADHS summarized the main points of the article by lifting various quotes. It is very telling that ADHS shortened one of the sentences they quoted. The bit about microwave sickness was removed from this sentence:

> "Research in populations near cell phone base stations in Europe indicates that some people living within about 300 metres of a base station are more likely to experience symptoms, such as headache, memory changes, dizziness, tremors, depression and sleep disturbance, that are similar to a condition known as "microwave sickness"."

In the ADHS version of the above quote, the last part of the sentence – "that are similar to a condition known as "microwave sickness" – has been removed.

God forbid a condition known as microwave sickness should be allowed to percolate in the brain of anyone reading the ADHS study. They might actually look it up and find that, in addition to thousands of articles and references to it, Merriam-Webster's medical dictionary defines it as:

> "a condition of impaired health reported especially in the Russian medical literature that is characterized by headaches, anxiety, sleep disturbances, fatigue, and difficulty in concentrating and by changes in the cardiovascular and central nervous systems and that is held to be caused by prolonged exposure to low-intensity microwave radiation."

People might actually begin to wonder why there was no in-depth discussion of that condition in the ADHS study, or even any mention of it. Worse, they might even recognize some of the symptoms as their own and realize what the heck has been degrading their health and then demand something be done about it. Oh wait, we did that, and that's why this ADHS study was concocted – I mean, conducted – in the first place!

ADHS also left this TPH statement out of their summarized main points: "There is agreement that biological (i.e. non-thermal) effects from radiofrequencies are evident from research with animals, cell cultures and in humans."

I would say that's important enough to include as a key point in a study about the health effects

of "smart" meters, wouldn't you?

Here is ADHS' incredibly dishonest response to the TPH report:

> "Although this article infers the biological feasibility of RF exposure and nonthermal effects, this article does not directly relate to the goals of this review. ADHS focused on RF exposures in the home. RF exposure at or near cell towers tend to be at much higher power densities than that which are measured near electronic meters, and is therefore not within the scope of this report."

Say what? The article "infers biological feasibility of … nonthermal effects"?

The article did not "infer" anything. It was clear. The author came right out and said it: **"There is agreement that biological (i.e. non-thermal) effects from radiofrequencies are evident from research with animals, cell cultures and in humans."**

Shame on ADHS for attempting to deceive Arizonans with that blatant misrepresentation.

And did you note the beautiful irony? ADHS says, "... this article does not directly relate to the goals of this review." Ha! Of course the article doesn't if it claims that "biological (i.e. non-thermal) effects from radiofrequencies are evident."

That should make anyone wonder what the real goals of the ADHS study are. It looks to me like ADHS tipped their hand, and that the real goals of their study were to whitewash microwave sickness and provide liability cover to the Arizona Corporation Commission and the monopoly utilities.

More irony: if "RF exposure at or near cell towers tend to be at much higher power densities than that which are measured near electronic meters", then would it not make sense to be concerned about additional sources of microwaves being added to those areas near cell towers? Shouldn't that be "within the scope of this report"? Instead, ADHS just blew the whole thing off.

And speaking of blowing things off, I was almost left speechless at how ADHS blew off the third and final report in their "Submissions from the Community" section. ADHS is either incredibly stupid or incredibly corrupt to have dismissed this report for the reason they gave.

Dr. Andrew Goldsworthy's "The Biological Effects of Weak Electromagnetic Fields Problems and solutions" is a masterpiece and must reading for anyone with an interest in this subject. (http://www.cellphonetaskforce.org/wp-content/uploads/2012/04/Biol-Effects-EMFs-2012-NZ2.pdf)

Goldsworthy "... is a retired lecturer from Imperial College London, which is among the top three UK universities after Oxford and Cambridge and is renowned for its expertise in electrical engineering and health matters. Dr Goldsworthy spent many years studying calcium metabolism in living cells and also how cells, tissues and organisms are affected by electrical and electromagnetic fields." [from the study's Foreword]

For anyone – anyone except ADHS, that is – who reads Goldsworthy's report, it will be obvious that the report is about how microwaves affect people at the cellular level. Goldsworthy explains how

that is done; he explains the mechanism of harm. All sorts of microwave sources are discussed – cell phones and towers, WiFi, DECT phones, and "smart" meters.

In the course of his report, Goldsworthy mentions frequencies between 6 and 600 hertz twice. He never calls that frequency range "radiofrequency" or "RF" – because it isn't. It's clear that ADHS does not understand frequency modulation or inter-cellular communication and so did not understand Goldsworthy's report at all. In short, Goldsworthy's report is way, way over their heads. In another one of their mistaken "gotcha" moments, ADHS seized on something they did not understand and mistakenly used that to dismiss Goldsworthy's report altogether.

Here is how ADHS dismissed Goldsworthy's 29 page report:

> "ADHS Response: This article references RF between 6 Hz and 600 Hz. However, the range of RF is actually 3KHZ to 3GHz. EMF in the range of 6 Hz and 600 Hz is actually Extremely Low Frequency (1-300Hz) and Intermediate Frequency (IF) Fields (300 Hz - 10 MHz). This review focused on RF and did not research the potential health effects of ELF or IF."

Poor ADHS had no idea what they were doing. Modulation of the carrier wave by other frequencies is needed for data communication. That's how this stuff works!

I contacted Dr. Goldsworthy and asked for his take on the ADHS response. Below is his reply in full:

> Dear Warren
>
> Thank you for your email.
>
> I have checked Page 22 of my article and it appears that ADHS have completely misunderstood it. The ELF frequencies that I referred to are not the actual microwave frequencies emitted by the device. They are instead the frequencies with which the microwaves are modulated; i.e. the frequencies of the pulses that carry the information.
>
> They are damaging because the cell membrane can demodulate the signals so that the harmful ELF frequencies are extracted (in principle, it is like the way in which radio set demodulates radio-frequencies to give the audio frequencies that you hear from the loudspeaker). I have explained a mechanism by which this can happen in the Section on demodulation on Page 19).
>
> However, whatever the mechanism, there are ways to overcome most of the biological effects of the modulation, either by burying them in low frequency random noise or by using a "balanced signal" in which the effect of the modulation is cancelled out by transmitting a signal that is pulsed 180 degrees out of phase on a second microwave carrier. As far as the phone company is concerned, its like two separate phone calls because they are on different microwave frequencies. but as far as the body is concerned, the modulation frequencies are added together and because they are of opposing polarities, they cancel each other out.

Of course, smart meters are likely to be more damaging than cell phones because they are transmitting their pulses 24/7.

I hope this helps.

Best Wishes.

Andrew

In addition to completely misunderstanding studies, misrepresenting them and dismissing them out of hand, another aspect of the "Submissions from the Community" portion of the ADHS study – and one of its major failings – was ADHS's treatment of individuals who reported health damage from "smart" meters.

Rather than thoroughly investigate and test these individuals, ADHS simply listed their health complaints and dutifully tabulated and quantified them. One table may be found in the "Submissions from the Community" portion, and the complete table is in the corresponding Appendix A.

ADHS did not contact any of the "smart" meter victims. The list of "smart" meter victims came only from those who had complained at the ACC docket. There was no statewide publicity of the ADHS study so that other "smart" meter victims could tell their story. There was no 800 number for anyone to call. There were no health surveys. No communities were surveyed with simple symptom related questions. No blood work done along the lines of what Dr. Klinghardt is doing in Seattle where he has isolated specific inflammatory markers in people's blood who are exposed to "smart" meter radiation. (Go to the 29:30 mark in this YouTube video of Dr. Klinghardt for the information ADHS missed: https://www.youtube.com/watch?v=b_wxM6IAF1I)

ADHS could have looked at the state's death rate since "smart" meters have been installed. One does not have to be an epidemiologist to notice a large increase since "smart" meters have been installed. I know for a fact that neurologists in Flagstaff and Cottonwood are overloaded. In Flagstaff it is so bad that only the worst cases get an appointment. Why are these things happening? What has changed? ADHS never asked so ADHS will never know.

In short, a health study that only examines the health of the meters and not the health of the people is worthless.

Field Study Follies – more incompetence

Questions of accuracy arise in the "Field Study" part of the ADHS study.

It is hard to believe that the Arizona Radiation Regulatory Agency (ARRA), who measured "smart" meter microwave emissions for the ADHS study, got accurate readings.

ARRA was measuring at one foot away from AMI ("smart") meters and the highest reading they got was 1450 microwatts per meter squared? (Watts per meter squared is the unit of measurement ARRA used. I use microwatts per meter squared so I will be converting the ARRA measurements by

multiplying by 1,000,000).

Despite the fact that I usually do not measure "smart" meters at that close a distance, still I get readings much higher than what ARRA measured. So since signal strength drops with distance, the ARRA measurements make no sense.

See my YouTube videos **APS Caught Lying** and **APS Caught Lying Again** for examples of my "smart" meter measurements.

It may be that ARRA did not measure enough "smart" meters. 17 "smart" meters is a very small sample.

I *have* found a few "smart" meters that are very weak (despite the APS claim that they all transmit at the same strength). Nevertheless, it still seems doubtful that out of 17 meters the strongest signal would be only 1450 microwatts per meter squared at as little as one foot away.

A more likely explanation is that the Tenmars TM-195 measuring device that ARRA used is cheap and inaccurate. My friends and I who have more expensive, accurate and sophisticated measuring equipment laughed when we saw that ARRA was using a $135 device. For comparison, the Gigahertz Solutions HF35C that you can see me using in my videos was almost $500 (with attenuator). Friends of mine have equipment in the thousands of dollars.

The Tenmars antenna is omnidirectional. A device with a directional antenna would have been more appropriate and accurate for measuring "smart" meters.

Put more technically by Richard Tell in one of the Vermont studies that ADHS promoted and claimed to have actually used in establishing their "field sampling plan":

> "Measurement data can be distorted when using an isotropic probe to measure steep spatial gradients close to a radiating element of a smart meter."

Based on that Tell comment that ADHS supposedly read, and based on the following features listed in the Tenmars owner's manual, the Tenmars is therefore an incorrect device to use for measuring "smart" meters:

- For isotropic measurements of electromagnetic fields.
- Non-directional (isotropic) measurement with three- channel measurement sensor.

In short, the HF35C with directional antenna that I use is a correct device for measuring "smart" meters. The Tenmars that ARRA used is not.

Additionally, the Tenmars makes no sound so the user cannot really be sure what they are measuring. My HF35C makes different sounds for different sources of microwave. There's no guessing.

One of the measuring professionals in Arizona wrote me that, "The Tenmars TM-195 RF meter is only accurate on continuous RF emissions. It performs poorly on pulsed radiation emissions. I

consider all RF testing in this report to be inaccurate and therefore invalid. It shows incompetence by the people involved with the report."

Having used a Tenmars TM-195 myself, I disagree with him. The Tenmars TM-195 is never accurate.

At best, the Tenmars is an amateur grade device suited for a homeowner on a budget who wants general readings around the house. It is *not* suitable for a serious study. In a cynical sense, the Tenmars was the perfect choice for the ADHS study – a pitifully inadequate meter for a pitifully inadequate study.

Call a couple of the listed companies that measure professionally in Arizona. I have. They want around $2,000 per day. They aren't using a Tenmars TM-195.

In addition to using an improper device, ARRA measured at an improper distance. Because the emitted wavelength of a "smart" meter is longer than 1 foot, it is best to measure at a greater distance than one foot.

Of course even if ARRA got measurements equal to mine, those measurements would still be under the FCC guidelines. That was never the issue anyway since the antiquated and dangerously inadequate FCC "guidelines" are part and parcel of the entire "smart" meter health problem.

Indeed, much of the "Field Study" section of the ADHS study, because it is centered around those guidelines, exposes how ridiculous those guidelines are. For example, in discussing how compliance with the FCC was met, ADHS wrote, "The 30-minute averages were calculated by using the top six 5-minute averages from a sampling location. This approach provided an estimation of the possible maximum 30-minute exposure throughout a day."

But a day is 24 hours, not 30 minutes. ADHS does not understand chronic exposure, nor does the FCC.

ADHS explains that, "FCC, ICNIRP and IEEE guideline values was [sic] determined based on established adverse thermal health effects. The purpose of these guidelines are to prevent whole-body heat stress and excessive localized tissue heating." ADHS then goes to show that their 30 minute averages of "smart" meter emissions are well below those values.

Even though they listed all the symptoms of "smart" meter victims, it obviously never occurred to ADHS that "smart" meter victims never complained about "whole-body heat stress" or "excessive localized tissue heating."

ADHS wrote, "FCC does not have an established standard for non-thermal health effects because of insufficient information." Actually industry lobbying, military influence, corruption and regulatory capture are the real reasons. "Insufficient information" has nothing to do with it. For how it all began, read the book, *The Zapping of America*. And incidentally, the current chairman of the FCC, Tom Wheeler, was a career lobbyist for the cable and wireless industry, so don't look for the FCC to find "sufficient" information any time soon.

ADHS then launches into the usual series of wiggle words to explain why we shouldn't worry about "smart" meter radiation:

> " Our review of US and most internal government assessments, and scientific publications indicated that there is **no consistent or convincing evidence** to support a cause-and-effect relationship related to the exposure to the RF frequency (900 - 930 MHz) used by the smart meters."

No "consistent" evidence? **—> So there is in fact evidence.**

No "convincing" evidence? **—> Convincing to whom?**

ADHS:

> "The majority of the scientific studies concentrated on the possible health effects from mobile phone exposure. **When compared to mobile phones, smart meters represent lower RF exposure sources** because of the attenuation factor of the building structure (for example: walls), and the distance from radiation signal source (i.e. location of the smart meters and mobile phones in relation to the human body.)"

Once again, ADHS displays their lack of understanding of chronic exposure. "Smart" meters *do not* represent lower RF exposure sources than cell phones. "Smart" meter emissions are 24/7. Cell phone use is intermittent and voluntary.

In an incredible admission of incompetence, ADHS stated, "We do not have access and do not have the ability to review the original paper (in Russian). The source indicated that this value was set based on an animal study consisting of 110 rats exposed to 900 and 1,800 MHz at 5 and 20 W/m2."

What "source"? None is mentioned or footnoted. ADHS does not have "the original paper" but even if they did they couldn't read it because it's in Russian? Honestly, that is just shamelessly sloppy. Ever hear of a translator, ADHS? You don't even need to pay a human being to do it. Here's some free software: http://translation.babylon.com/russian/to-english/

ADHS stated: "ADHS used the Russian standard as a comparison to ARRA's measurements. The results showed that none of the overall average readings of AMI (ranging from 0.000025 to 0.000888 W/m2) or AMR (ranged from 0.000016 to 0.000377 W/m2) meters exceeded the standard (Table 6.)"

The more accurate "smart" meter measurements that I have taken *do* in fact exceed the Russian standard.

In their brief discussion of "smart" meters that do not transmit via microwaves but transmit over existing power lines – Power Line Communication (PLC) – ADHS manages to get that wrong once again. ADHS says, "During the data transmission process, a power frequency field of 60 Hz is produced." Uh, no, 60 hertz is always present on line. Always. PLC does not produce the 60 hertz field.

For more information about power line frequency, ADHS directs us to a publication prepared by the National Institute of Environmental Health Sciences called "EMF: Electric and Magnetic Fields

Associated with the Use of Electric Power." Had ADHS actually been able to comprehend this very simplistic document, they would have learned on page 6 that "Electricity in North America alternates through 60 cycles per second, or 60 Hz." PLC is *not* what's causing that. (http://www.niehs.nih.gov/health/materials/electric_and_magnetic_fields_associated_with_the_use_of_electric_power_questions_and_answers_english_508.pdf#search=Electric and Magnetic Fields Associated with the Use of Electric Power)

Conclusion – "smart" meters are not found safe

So after all the blatant blunders and bias, the reliance on flawed and corrupt institutions and studies, after all ADHS' inability to understand the basics, after all the wiggle words, seemingly deliberate misrepresentations, obvious omissions and data cherry picking, ADHS announced to Arizona that "***Exposure to electric meters (AMI and AMR) is not likely to harm the health of the public.***"

How can anyone believe them? And even if anyone did, what kind of assurance is "not likely to harm"?

Did we ever hear that about analog meters, that they are "not likely to harm"? No, we didn't.

Note the state statutes:

- **A.R.S. 40-361.B** – Every public service corporation shall furnish and maintain such service, equipment and facilities as will promote the safety, health, comfort and convenience of its patrons, employees and the public, and as will be in all respects adequate, efficient and reasonable.

- **A.R.S. 40-321.A** – When the commission finds that the equipment, appliances, facilities or service of any public service corporation, or the methods of manufacture, distribution, transmission, storage or supply employed by it, are unjust, unreasonable, unsafe, improper, inadequate or insufficient, the commission shall determine what is just, reasonable, safe, proper, adequate or sufficient, and shall enforce its determination by order or regulation.

In particular, note that A.R.S. 40-321.A *does not* say "the commission shall determine what is just, reasonable, likely not to harm, proper, ..."

"Not likely to harm" *does not* equal safe. Safe is safe. "Not likely to harm" is a gamble, gambling with the health of the public, conducting an experiment on the public.

According to Merriam-Webster's dictionary safe means:

1. not exposed to the threat of loss or injury
2. providing safety
3. unlikely to provoke controversy or offense
4. having or showing a close attentiveness to avoiding danger or trouble

5. not causing or being capable of causing injury or hurt
6. worthy of one's trust

"Not likely to harm" does not fall within the definition of safe.

Note especially definition # 1. It *does not* say "not *likely* exposed to the threat of loss or injury."

Note especially definition # 2. It *does not* say "*likely* providing safety."

Note especially definition # 5. It *does not* say "not *likely* causing or being capable of causing injury or hurt."

Safe is not a wiggle word. No one should attempt to redefine it.

As slipshod as the ADHS study is, their "Not likely to harm" classification places wireless "smart" meters, the utilities who use them, and the Arizona Corporation Commission (ACC) who sanctions them, outside of the law.

"Smart" meters have not been found safe and must be removed. Now!

Wiggle your way out of that, ACC.

Friday December 12, 2014
ACC Office @ 1200 W. Washington St.

Michael Johnson email: mjohnsonmw1@gmail.com
Sedona. AZ

MY TOP 5 REASONS AGAINST SMART METERS and OPT OUT FEES

5) The mayor and city council of Sedona voted to ban Smart Meter installation on all city-owned buildings.

4) According to Mr. Warren Woodward, the Arizona Department of Health and Safety used a $135 Tensmar TM-195 meter in its study of Smart Meter signals and exposure. By default, the study is tainted and unreliable. Further, Babara Litrell reports in Sedona BIZ that ADHS reported Smart Meters "not likely to harm" public health. This is not good enough. (see item 4)

3) Lloyd Burrell – a guest on Republic Broadcasting Network Radio - reported that the World Health Organization said Smart Meters running day and night can increase risk of cancer and other diseases. (see item 3)

2) Smart Meters are causing fires throughout United States as well as other countries. (see item 2)

1) My number one reason against Smart Meters and opt out fees is I never opted in for a horrible potential danger. Therefore, I should not have to pay APS to opt out.

0) And last in 1919, before Hitler was the WWII Hitler we know, he said "A man who knows a thing, who is aware of a given danger, and sees the possibility of a remedy with his own eyes has the duty and obligations, by God, not to work silently, but to stand up before the whole public against the evil and for its cure."
I'm asking you to "stand up" and not enable the "evil" of APS charging opt out fees!

ITEM (4)

Letter to The Editor: ADHS report raises questions
by Sedona.biz Staff

By Barbara Litrell, Sedona Resident
(December 11, 2014)
Determining that Smart Meters are "not likely to harm" public health does not fulfill the mission of ADHS to protect the health of Arizona's children and adults.
For years the tobacco industry covered up its knowledge that smoking was harmful to health until, in 1964, the Surgeon General, based on epidemiological evidence, declared smoking can cause cancer and required labeling and regulated advertising. Read more of this post (not included)

(MY NOTE)
This is like General Motors saying ignition switches in newer cars are not likely going to cause harm. But, they did and GM admitted later what they knew earlier. And now the State of Arizona is suing GM for their failure of concealing this information. Will APS be next?

(Item 3).
FROM Lloyd Burrell.
guest on Republic
Broadcasting Network
Radio

Smart Meters And Dirty Electricity

The other little know fact about smart meters is that typically they use switched mode power supply (SMPS). SMPS is supposed to offer better efficiency and reduced cost in conversion of electrical power. Unfortunately it is also responsible for creating 'noise' on house wiring, otherwise known as dirty electricity.

This is no small detail. For my recommendations on dealing with dirty electricity please click here.

What To Do If Your Utility Company Wants To Install A Smart Meter

If you don't currently have a smart meter installed in your home but you find out your utility company is going to install one, there are several things you can do. See this article for information on the steps you can take.

Take Action Now

The World Health Organization has listed smart meter radiation as a possible carcinogen. This means that your smart meter, that's on all day and night-all throughout the year, can increase your risk of cancer and other diseases. It's time to get informed and take appropriate measures to protect your loved ones. Take action now!

It is difficult to understand why are utility companies are so intent on installing wireless smart meters when smart meters could do just the same job but much more safely by being connected to a regular telephone line.

Smart Meter Help Resources

For more information on steps to take if your utility company wants to install a smart meter read here.

Click here to submit your complaint online about smart meters.

But, **smart meter radiation is only part of the problem**, Click here if you are interested in learning more about EMFs and what you can do about them.

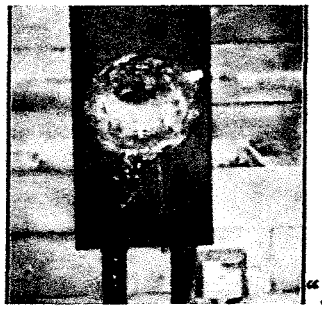
(ITEM 2)

Smart Meter Fires and Explosions

The following is a compilation of reports from the US , Australia and Canada about fires, explosions, electrical problems or burned out appliances due to Smart Meter installations. If you have experienced similar problems, please post your story in the comment section below.

The US Consumer Products Safety Commission (CPSC) is a federal agency that will take complaints on utility smart meters from all US states. If you have or had smart meter electrical or fire problems CALL: *(800) 638-2772* *Monday through Friday from 8:00 a.m. to 5:30 p.m. ET or submit your complaint by email.*

Smart meters catch-fire when it rains



"...an independent review in Canada revealed that smart meters are experiencing catastrophic failures when **rain water** (and/or condensation along with other contaminants) gets into the smart meters themselves, causing arcing across electronic components with eventual failure of the meter.

Well, last night it rained in Regina, Saskatchewan, and there was another smart meter fire.

SaskPower confirmed crews were called to replace yet another failed smart meter on a resident's home on Regina's east side early Friday morning."

10/6/2014 Couple Escapes fire, Dogs Dead, Blames Smart Meter

A couple escapes a house fire in Detroit. Sadly, their two dogs died in the blaze.

more info online

German ambassador in
"two hoots" about the
But the demilitarization of
both Versailles and Locarno.
talks with Nazi officials for
air and naval forces. In
the Rhineland, or what the
obstacle that Wedemeyer's

Colonel de Gaulle pointed
were commanded by old
moved at 40 mph or
had been replaced by
effect than a cause.
behind her frontier fortress
strategy that she would
case by case, crisis by
neither diplomacy nor
of a changing world was

before the cheering
foreign offices of Paris
Hitler invented a region
Czechoslovakia and demanded
Lord Halifax reminded
applied to French frontiers.
democratically elected govern-
dismemberment. The Italian
initiating an accord on
British and French swallowed
In March 1939 Hitler's

appeasement as their Prime
Neville Chamberlain's govern-
allies had been demanding
about. What the Paris
was belatedly recog-
Britain's unilateral guarantees
Poland and Romania.
Hitler's arms, for Stalin
and Romania.

(ITEM -0-)

With the signing of the Nazi-Soviet Pact in August 1939 war was inevitable. Britain was obliged to go to war over Danzig.

Churchill well describes the unhappy scene at Tours on 13 June 1940 – the bomb craters, the refugees, the sullen faces of French officialdom, the 'spring and sunlit garden' of the prefecture – where he solemnly appealed to the French Prime Minister, Paul Reynaud, that he was 'not in a position to release France from her obligation' and allow her to seek a separate peace with Germany. 'Our war aim remained the total defeat of Hitler and we felt that we could still bring this about.'[26] But how far back did that 'obligation' go? To Paris in 1919? To Locarno in 1925? Many Frenchmen would have dearly loved that to have been so. In fact, the 'obligation' had been cobbled together by Chamberlain and Reynaud on 31 March 1940, six weeks prior to the German invasion of France.

3 Heartlands in the East

That war began in the mind of one man in the summer of 1919. The peace treaty between Germany and the Allies had just been signed at Versailles. Adolf Hitler had joined the 'Information Department' of the army forces that had crushed a Soviet Republic in Munich and he had made a discovery: 'I could speak!'[27] In the autumn and winter he was harangueing the crowds in Munich's beer halls on such subjects, he relates in *Mein Kampf*, as 'War Guilt' ('which at that time nobody bothered about') and the 'Peace Treaties'. 'Nearly everything was taken up that seemed agitationally expedient or ideologically necessary,' noted Hitler.[28]

Indeed, his ideology developed with the crowd in a kind of spiralling exchange, like a Baptist minister with his congregation. Hitler wanted the truth told, and no secrets kept. He contrasted the 'manly forthrightness' of the speaker on the tavern table with the 'cowardly swindlers' who worked in the 'darkness of silence'. 'A man who knows a thing, who is aware of a given danger, and sees the possibility of a remedy with his own eyes,' said Hitler, 'has the duty and obligation, by God, not to work "silently", but to stand up before the whole public against the evil and for its cure.'[29] A recurring theme in Hitler's speech was the need for interchange between the 'inner' and the 'outer': between the 'inner' thought and the 'outer' expression, the 'inner' vision of the inarticulate crowds and the 'outer' words of the orator on the table; the 'inner' unity of the national will and its 'outer' freedom.

This would determine his approach to foreign policy. 'Without the recovery of our external freedom,' he wrote, or rather dictated, in 1924,

FROM THE BOOK; 1945 The War that Never Ended

* "stand up" and do not enable APS by allowing any opt out fee.

Use of directories and route usability. You ar

From: Denise Harkison <denise.harkison@gmail.com>
Subject: **Fwd: Trees near a smart meter**
Date: December 11, 2014 5:06:31 PM MST
To: Judy Staab <judystaab@earthlink.net>, Doug Staab <dstaab@earthlink.net>
▸ 2 Attachments, 4.5 MB

---------- Forwarded message ----------
From: **Sam** <lilchooblie@gmail.com>
Date: Thu, Dec 11, 2014 at 3:01 PM
Subject: Trees near a smart meter
To: denise.harkison@gmail.com

Sent from my iPhone

I contend that the report set forth by the ADHS concerning smart meter safety is both fraudulent and severely lacking in subjective or accurate test data. The ADHS has had almost a year to study the effects of smart meters on humans and animals, and all they have issued are excerpts from numerous reports with what clearly appears to be information cherry picked to back up their conclusions.

The data used and quoted by the ADHS has been found to be out of date, and in complete non-conformity to the ANSI standards as set forth for in IEEE C95.1.

Therefore, all data contained within the body of the ADHS report which is based on these standards should be considered null and void and thus potentially puts the commission and the state of Arizona in a liability position for all health related issues which should be avoided.

About ADHS

The Arizona Department of Health Services ***promotes and protects the health of Arizona's children and adults.*** Its mission is to set the standard for personal and community health through direct care, science, public policy, and leadership.

I would like to set the record straight on the report generated by the ADHS. First off, they have deliberately chosen to violate the very mission statement they allegedly operate under, by publishing a report based on information that is not current. Had they done their due diligence (of which they have had more than a year) they would have drawn their conclusions based on accurate and up to date data.

I appreciate the Commissions time in allowing me to break this alleged study apart paragraph by paragraph to expose the truth of what they deliberately left out of their report to allow this dangerous technology to continue, thus putting the state, the commission and all people of this state at risk.

As this will clearly show, acceptance of this report will potentially put a severe liability on the both the Commission and the state for the health issues these meters are known to create. Couple that with the known fire issues directly attributed to certain smart meters and the potential for class action lawsuits increases exponentially.

I do believe that the following questions posed need to be answered before any consideration of this report is accepted:

Since reliable information requires data logging over a specified period of time to be considered accurate:

1) Where within the study does it show or provide any readings that were taken, recorded and logged over a 24 hour Time Weighted Average (TWA) period?
2) Were any of the studies conducted at locations of those citizens who have expressed concerns to the ACC or have been directly affected by these meters?
3) Where are the reports and documentation for all the readings taken over:
4) A 48 hour TWA period?
5) A 72 hour TWA period?
6) A 96 hour TWA period?
7) A week, a month, several months since the ADHS started this study?
8) How is that consumers appear to have spent more time researching the truth than the ADHS did?

9) How is it that a simple review of the laws and statutes quoted by the ADHS has been found to be both inaccurate and ineligible for consideration – especially when they had over a year to perform their research?

In reading the ADHS report, I cannot find any of this information within the body of their published report that was submitted as "findings and conclusions".

Unfortunately, It is not rocket science to see that the report is at best incomplete and definitely incompetent in its conclusions based on the manner in which it has been performed.

It therefore, should be rejected by the Commission and an immediate independent study conducted by those within the environmental medical community with a background in the field of radiation contamination that has been approved by a panel of consumers and commissioners in a meeting to be held in the near future.

It is my intent to address each paragraph as written and submitted by the ADHS to the commission with the facts found and not just surmised.

I appreciate your indulgence in reviewing these findings, as it is way too important to the people of Arizona to rush to judgment using a report that can only be considered fraudulent at best.

Introduction

A "smart meter" is a term that typically refers to electronic meters that have a two-way communication function between the utility company and the customer. Arizona citizens have been concerned about the potential health effects from exposure to radiofrequency (RF) emitted from Smart Meters. In order to address the customer concerns, the Arizona Corporation Commission (ACC) has requested a review of smart meters used in Arizona. This review is to include a survey of meters used in Arizona to determine whether they emit RF within the Federal Communications Commission (FCC) guidelines, and an evaluation on the potential health risks of RF radiation from the smart meters. In Arizona, there are multiple metering technologies used, and not all types will have and/or utilize the two-way communication function. For the purpose of this report, Arizona Department of Health Services (ADHS) will refer to all wireless communicating meters as electronic meters, regardless of the communication function. The ACC provided comments on the goals and scope of this project, but relied on ADHS and the Arizona Radiation Regulatory Agency (ARRA) for their areas of expertise. The Environmental Toxicology Program in the Office of Environmental Health at the Arizona Department of Health Services conducts risk assessments to determine potential public health impact from site-related contamination. At the request of other agencies or the public, the Environmental Toxicology Program reviews available environmental and exposure data to evaluate potential community exposures to hazardous substances. ADHS does not collect new environmental data, but instead, relies on other agencies or third parties to collect the data.

According to the available documentation, the review originally requested by the ACC, clearly directed the Arizona Department of Health Services to conduct a study into the health concerns expressed by numerous customers throughout the state on the health effects directly attributed to smart meters.

According to their "Introduction", they state that "The Environmental Toxicology Program of the Office of Environmental Health at the Arizona Department of Health Services conducts risk assessments, to determine potential public health impact from site related contamination." If that is indeed the case, then how do they explain away what precautions are listed worldwide concerning microwave non-ionizing radiation?

Many of the studies conducted by the government are later proven to be inaccurate. As consumers and the Commission as legislators or consumer advocates, we're supposed to have a certain degree of common sense to use in judgment.

The rest of the world has deemed these meters and the so non-ionizing radiation they produce to be dangerous to human health; why didn't the ADHS study come to the same conclusion?

I would ask that the Commission consider the hundreds of lawsuits attributed to drugs allegedly tested and approved by the FDA (a federal government agency) that have been pulled off of the market, and are currently undergoing lawsuits for the fatalities and health issues they produce, does the state want to find themselves in that situation as well?

Since the ADHS has called upon the Arizona Radiation Regulatory Agency for input, I thought it very beneficial in proving that the data required by this agency has not been met by either of the utilities as per state documented requirements.

ARRA houses the nonionizing radiation section, which enforces Arizona Administrative Code Title 12 Chapter 1, Article 14 "The Control of Nonionizing Radiation." These rules address sources of radiofrequency radiation (RF) in the environment, occupational exposure concerns, as well as public exposure. ARRA regulates Class 3B and Class 4 lasers used in the medical, industrial and light show fields, Ultraviolet radiation in tanning facilities, RF radiation sources such as heat sealers and industrial oven, RF radiation in the industrial environment within a frequency range of 0.3 megahertz (MHz) to 100 gigahertz (GHz), and communication sources through a registration/license program. ARRA does not have regulatory authority to enforce rules regarding electronic meters. However, they have the expertise, experience, and ability to measure RF emitting devices including electronic meters.

Since the ADHS decided to use the ARRA as a testing agency and as a reference whom they classified as experts, let's examine their criteria closely as found in the referenced Title 12, Chapter 1, Article 14.

Since the only information that is relevant to this study is that of what the ARRA describes as "Nonionizing radiation sources and standards for nonionizing radiating", one has to ask the Commission:

1) Where is the copy of the utilities individual registration posted and recorded as required by the ARRA for use of a nonionizing radiation device (smart meter) posted?
2) Where are ALL the permits required for every device installed?
3) Does the Commission have a copy available for public review?
4) Has the ACC even seen this documentation; or are they aware of the requirement for it?

Staying on point, article E also clearly states that: "A person who is operating more than one facility, where one or more nonexempt nonionizing sources are used, shall apply for a separate registration for each facility".

Since each and every home, apartment and business equates to being a separate facility, then where has APS applied for and posted each of these facilities registration certificates with the agency and the commission?

The following excepts are taken verbatim from the ARRA website:

TITLE 12. NATURAL RESOURCES

CHAPTER 1. RADIATION REGULATORY AGENCY

ARTICLE 1. GENERAL PROVISIONS

R12-1-101. Scope and Incorporated Materials

A. Except as otherwise specifically provided, this Chapter applies to all persons who receive, possess, use, transfer, own, or acquire any source of radiation.

ARTICLE 14. REGISTRATION OF NONIONIZING RADIATION SOURCES AND STANDARDS FOR PROTECTION AGAINST NONIONIZING RADIATION

R12-1-1401. Registration of Nonionizing Radiation Sources and Service Providers

A. A person shall not use a nonexempt nonionizing radiation source, unless the source is registered by the Agency.

E. A person who is operating more than one facility, where one or more nonexempt nonionizing sources are used, shall apply for a separate registration for each facility.

F. A person in the business of installing or servicing nonexempt nonionizing sources shall apply to the Agency for registration 30 days ***before furnishing the service***. The person shall apply for registration on a form furnished by the Agency and shall provide the information required by A.R.S. § 30-672.01.

R12-1-1402. Definitions

General definitions

"Nonexempt nonionizing source" means any system or device that contains a nonionizing source listed in R12-1-1302(F). "Operator" means a person who is trained in accordance with this Article and knowledgeable about the control and function of a nonionizing device regulated under this Article.

(R12-1-1302. License and Registration Categories

F. Category F registrations are those that register nonionizing radiation producing sources regulated under 12 A.A.C. 1, Article 14. The Agency shall not combine Category F registrations with any other registration

12. An "other" nonionizing radiation device authorizes the operation of a nonionizing radiation device or other device not included in any other category specified in subsection (F).

Radio frequency and microwave radiation definitions:

"Accessible emission level" means the level of radio frequency radiation emitted from any source, expressed in terms of power density in milliwatts per square centimeter or electric and magnetic field strength, as applicable, and to which human access is normally possible.

"Far field region" means the area in which locally uniform distribution of electric and magnetic field strengths exists in planes transverse to the direction of propagation. The far field region is presumed to exist at distances greater than $2D2/\lambda$ from the antenna, where λ is the wavelength and D is the largest antenna aperture dimension.

"Maximum permissible exposure MPE" means the rms and peak electric and magnetic field strengths, their squares, or the plane-wave equivalent power densities associated with these fields and the induced and contact currents to which a person may be exposed without harmful effect and with an acceptable safety factor.

"Near field region" means the area near an antenna in which the electric and magnetic field components vary considerably in strength from point to point. For most antennas the outer boundary of the region is presumed to exist at a distance $\lambda/2\pi$ from the antenna surface, where λ is the wavelength.

"Radio frequency controlled area" means any location to which access is controlled for the purpose of protection from radio frequency radiation.

"Radio frequency source" means a source or system that produces electromagnetic radiation in the radio frequency spectrum.

"Radio frequency radiation" means electromagnetic radiation(including microwave radiation) with frequencies in the range of 0.3 megahertz to 100 gigahertz.

"Root-mean-square (rms)" means the effective value, or the value associated with joule heating, of a periodic electromagnetic wave. The rms is obtained by taking the square root of the mean of the squared value of a function.

"Safety device" means any mechanism incorporated into a radio frequency source that is designed to prevent human access to excessive levels of radio frequency radiation.

R12-1-1403. General Safety Provisions and Exemptions

A. Based on consideration of the following factors, the Agency may waive compliance with specific requirements of this Article:

1. Whether compliance requires product replacement or substantial modification of a product's current installation, and

2. Whether the registrant provided information requested by the Agency to determine if there are alternative methods of achieving the same or a greater level of radiation protection.

B. The registrant shall:

1. **Ensure that any nonionizing source is operated by an individual who is trained and has demonstrated competence in the safe use of the source.**

2. **Provide safety rules to each individual who operates a nonionizing radiation source and determine whether the individual is aware of operating restrictions and procedures associated with the safe use of the source.**

2. Make, or cause to be made, any physical radiation surveys required by this Article.

4. Maintain the following records for three years for Agency review:
   a. Results of any physical survey or calibration required by this Article;
   b. Radiation source inventories;
   c. Maintenance, service, and modification records; and
   d. Incident reports of known or suspected exposure to nonionizing radiation that exceeds any MPE specified in this Article.

C. A registrant shall not operate a nonionizing radiation source unless the source complies with all of the applicable requirements of this Article.

Historical Note
Adopted effective April 2, 1990 (Supp. 90-2). Section heading amended effective January 2, 1996 (Supp. 96-1). Amended by final rulemaking at 11 A.A.R. 61, effective February 5, 2005 (Supp. 04-4).

R12-1-1404. Radio Frequency Equipment

A. A registrant shall operate a radiation source that emits radio frequency radiation in a radio frequency controlled area, in a manner that will prevent human exposure that exceeds the MPE specified in IEEE Std C95.1-1999, Institute of Electrical and Electronics Engineers Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3kHz to 300 GHz, 1999 edition, which is incorporated by reference, published by the Institute of Electrical and Electronic Engineers, Inc., 345 East 47th Street, New York, NY 10017, and on file with the Agency. This incorporation by reference contains no future editions or amendments. The registrant shall post each point of access into a radio frequency controlled area according to R12-1-1406.

B. If a registrant is required to operate a radio frequency source in a controlled area, the registrant shall employ visual or audible emission indicators that function only during production of radiation.

C. If a source of radio frequency emissions is physically separate from the source's means of activation by a distance greater than 2 meters, the registrant shall place a visual or an audible emission indicator at the source and the point of activation.

D. A registrant shall place each visual emission indicator so that the location of the indicator does not require human exposure to radio frequency radiation that exceeds the applicable MPE.

E. A registrant shall inspect each safety device designed to prevent human exposure to excessive radio frequency radiation for proper operation at intervals that do not exceed one month.

F. If a machine emits mechanically scanned radio frequency radiation, a registrant shall ensure that the machine cannot, as the result of scan failure or any other malfunction, cause a change in angular velocity or amplitude, allowing human exposure that exceeds the applicable MPE.

G. A registrant shall physically secure each radio frequency sources to prevent unauthorized use and tampering.

Historical Note

Adopted effective April 2, 1990 (Supp. 90-2). Amended effective January 2, 1996 (Supp. 96-1). Amended by final rulemaking at 11 A.A.R. 61, effective February 5, 2005 (Supp. 04-4).

R12-1-1405. Radio Frequency Radiation: Maximum Permissible Exposure

A. A registrant shall not expose a person to radio frequency radiation that exceeds the applicable MPE specified in IEEE Std C95.1-1999, Institute of Electrical and Electronics Engineers Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3kHz to 300 GHz, 1999 edition, which is incorporated by reference, published by the Institute of Electrical and Electronic Engineers, Inc., 345 East 47th Street, New York, NY 10017, and on file with the Agency. This incorporation by reference contains no future editions or amendments.

B. At frequencies between 300 kHz and 100 GHz a registrant may exceed the applicable MPE if exposure conditions can be shown by laboratory procedures to produce specific absorption rates (SARs) above 0.4 watts per kilogram, averaged over the whole body, and spatial peak SAR values above 8 watts per kilogram, averaged over 1 gram of tissue.

C. At frequencies between 300 kHz and 1 GHz, a registrant may exceed the applicable MPE, if the radio frequency input power to the radiating device is seven watts or less.

Historical Note

Adopted effective April 2, 1990 (Supp. 90-2). Amended effective January 2, 1996 (Supp. 96-1). Amended by final rulemaking at 11 A.A.R. 61, effective February 5, 2005 (Supp. 04-4).

R12-1-1408. Reporting of Radio Frequency Radiation Incidents

A. A registrant shall report in writing to the Agency within 15 days of a known or suspected personnel exposure to radiation that exceeds the applicable MPE incorporated by reference in R12-1-1405.

B. A registrant shall report to the Agency within 24 hours of a known or suspected personnel exposure to radiation that exceeds 150% of an applicable MPE incorporated by reference in R12-1-1405.

C. A registrant shall immediately report to the Agency a known or suspected personnel exposure to radiation that exceeds 500% of an applicable MPE incorporated by reference in R12-1-1405.

Historical Note

Adopted effective April 2, 1990 (Supp. 90-2). Amended effective January 2, 1996 (Supp. 96-1). Amended by final rulemaking at 11 A.A.R. 61,effective February 5, 2005 (Supp. 04-4).

R12-1-1409. Medical Surveillance for Workers Who May Be Exposed to Radio Frequency Radiation

A. Upon request by the Agency, a registrant shall provide a medical examination to an individual exposed to radiation reported to the Agency according to R12-1-1408.

B. A registrant shall provide a copy of the results to the Agency if an individual undergoes a medical examination, requested under subsection (A).

Historical Note

Adopted effective April 2,1990 (Supp. 90-2). Section heading amended effective January 2, 1996 (Supp. 96-1). Amended by final rulemaking at11 A.A.R. 61, effective February 5, 2005 (Supp. 04-4).

R12-1-1410. Radio Frequency Compliance Measurements

A. For obtaining measurements to determine compliance with R12-1-1405, the Agency shall use an instrument capable of measuring the field strength and frequency of radiation.

B. The Agency shall ensure that each instrument used for compliance measurements is calibrated every 12 months. The calibration shall be performed in a manner that meets the standards in IEEE Std C95.1-1999, incorporated by reference in R12-1-1404(A).

C. For compliance measurements of exposure conditions in the near field, the Agency shall obtain measurements of both the electric and magnetic field components. The applicable protection standards for near field measurements are the mean squared electric and magnetic field strengths (using the applicable MPE) referenced in R12-1-1405.

D. If the Agency is obtaining measurements to determine compliance in far field exposure conditions, the Agency may use measurements of power density in milliwatts per square centimeter or the calculated equivalent plane wave power density, based on measurement of either the electric

or magnetic field strength. The applicable protection standards are the power density values (using the applicable MPE) referenced in R12-1-1405.

E. In obtaining measurements in accordance with this Section, the Agency shall measure the electric and magnetic field strength:

1. Obtained at an emission frequency of 300 megahertz or less; and
2. Expressed in terms of power density.

F. For mixed or broadband fields at frequencies for which there are different protection standards, the Agency shall determine the fraction of the applicable MPE incurred within each frequency interval. To achieve compliance the sum of all the fractions shall not exceed unity (1).

G. The Agency shall obtain compliance measurements at a distance of five centimeters or greater from any object.

H. A registrant shall obtain measurements that are averaged over a six-minute period for pulsed and non-pulsed modes of radio frequency emission and make a correction for duty cycle in determining the average field strength.

The Institute of Electrical and Electronics Engineers, Inc.
345 East 47th Street, New York, NY 10017-2394, USA

Copyright © 1999 by the Institute of Electrical and Electronics Engineers, Inc.
All rights reserved. Published 16 April 1999. Printed in the United States of America.

Print: ISBN 0-7381-1557-6 SH94717
PDF: ISBN 0-7381-1558-4 SS94717

No part of this publication may be reproduced in any form, in an electronic retrieval system or otherwise, without the prior written permission of the publisher. IEEE Std C95.1, 1999 Edition (Incorporating IEEE Std C95.1-1991 and IEEE Std C95.1a-1998)

Based on the aforementioned requirements, it is apparent that both APS and SRP are in violation of numerous provisions detailed within the body of this rebuttal. If that is the case, then how could the ADHS come to the conclusions they did?

Specifically the violations identified within the body of this information are in accordance with Title 12; Chapter 1; Article 1; and listed as follows (all information highlighted in red above)

R12-1-1401 A, E and F

R12-1-1403 A2 – which clearly states “”whether the registrant provided information requested by the agency to **determine if there are alternative methods of achieving the same or greater level of radiation protection**.”

B2 and B4:

I would like to take this opportunity to address the Commission on this one requirement as set forth by the ARRA.

Since technology changes day by day, the Commission has the ability to allow consumers an alternative to the smart meter dilemma by granting the public the ability to purchase (at NO cost to the utilities) current devices which do the exact same thing a smart meter does, in that they monitor usage 24/7/365, remotely reports the data directly to the utility, and opens up the various rate plans to the public at large. Since the cost would be borne by the consumer, then no additional opt-out charges would apply for the use of a safe analog mechanical meter.

All in all it would be a win-win situation that everyone could live with. Information on the available equipment that meets the utilities requirements without harm to the public can be found at the end of the rebuttal.

The information referenced is the TED 5000C whole house monitoring system or the watt

R12-1-1404 B, C and E which specifically states that: "A registrant shall inspect each safety device designed to prevent human exposure to excess radio frequency radiation for proper operation at intervals that are not to exceed 1 month."

One would have to ask, since this is a clear violation of the Agencies requirement, how the ADHS did not address it in the body of their report? Further, since no inspections are performed at the required ARRA intervals, nor has the commission requested they be done; then the Commission would have to establish the baseline safety requirements. Since only a select few are certified by the Underwriters Laboratory (although ALL meters should be) then does that place the liability on the Commission or the utilities to assure that ANY meter used within the state is UL certified?

Since protection of the public at large is (according to state mission statements) paramount, then should not the Commission set the standards as to exactly what meters can be used? Should not the Commission and the ADHS err on the side of caution to protect the public? How many citizens need to come forth for the Commission to assure their protection? Are not ALL citizens of this state afforded the same protections under the law?

R12-1-1408A and B which states that: "A registrant shall report to the agency within 24 hours of a known or suspected personnel exposure to radiation that exceeds exceeds the applicable MPE incorporated by reference in R12-1-1405.

Since neither APS nor SRP have applied for, nor have been granted permits for the installation of any AMR meters, they are in violation of state law. Since they willfully violate the law, then they see no reason to report "suspected" exposure to the ARRA. This alone makes the ADHS report fraudulent or at the very least culpable in the violation of the law.

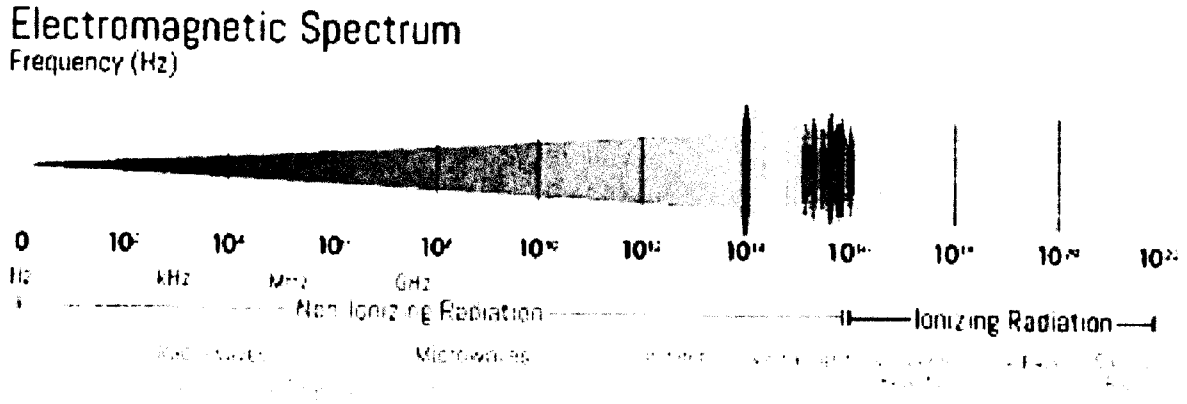
R12-1-1409 A and B which also states: "Upon request by the Agency, a registrant shall provide a medical examination to an individual exposed to radiation reported to the Agency according to R12-1-1408"

According to this requirement, then APS and SRP are directly responsible for providing a medical examination (at the complainants doctor of choice – NOT one appointed by the utility) to any individual exposed to microwave radiation produced by the AMI meters.

R12-1-1410A through H

Since the meters used for measuring the RF data are specifically required to be calibrated once a year for accuracy (section B), then the use of any "self-calibrating" device is therefore illegal for use or determining data. None of the sites used by the ADHS were of homes or locations of consumers who complined, then the data should be considered suspect as to the accuracy of the data collected.

Real data for the purposes of determining the amount of microwave radiation needs to be sampled at numerous locations, both inside and outside the home over a long term (I.E. 24 hours, 96 hours, 1 week, 1 month, 6 months) to safely come to any conclusion regarding the health issues raised by informed consumers. One CANNOT use data collected over several minutes to determine the actual amount of cumulative radiation exposure at any location.



The following information is also cited by the ADHS (by proxy) in that the IEEE levels they cite are directly tied to the conclusion they make. Below is a verbatim copy of the IEEE C95.1-1991 standards they quote. NOTE the last date available for approval closely!

IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz

Sponsor
IEEE Standards Coordinating Committee 28 on Non-Ionizing Radiation Hazards
Approved **8 December 1998**

IEEE-SA Standards Board

6. Rationale (pg. 27)

American National Standards Institute (ANSI) policy requires that each of its standards or guides be reviewed at 5-year intervals. At the time of expiration, the standard or guide may be reaffirmed, revised, or rescinded in accordance with the consensus of the reviewing body. In 1982, extensive revisions of the earlier standard were introduced into ANSI C95.1-1982 [B1] based on improved dosimetry that defined frequency-dependent limits on fields and power density. The use of SAR as the basic dosimetric parameter permitted the formation of exclusion rules. Since 1982, Subcommittee IV has met at least once, and usually twice, annually to review a wide range of proposed refinements of ANSI C95.1-1982 [B1]. The decision to expand the range of frequencies made it clear that quasi-static and quasi-optical considerations shall apply at the lower and higher boundary regions of the frequency range. ***Therefore, the applicability of SAR considerations was limited to the range from 0.1 MHz to 6.0 GHz, which includes the resonance range for human beings.*** Below 0.1 MHz, the database on electro-stimulation of biological tissue plays the dominant role and the primary dosimetric parameter is internal current density. Above 6.0 GHz, the exposures are quasi-optical, and under these conditions, power density is the meaningful parameter

Since these standards as set forth and used by the ADHS IAW IEEE C95.1-1991 are beyond the safe operational limits established by all other communities throughout the world, then they should have used standards which are up to date and currently accepted by the rest of the world community.

Since the ADHS chose to use the IEEE Std C95.1-1991; then by its own requirements stated above under section 6 "Rationale" is by the IEEE standard outdated, and more than three revisions behind in accordance with the ANSI requirement stated above. Thus making any reference to it invalid.

The goals of this report are 1) to determine whether RF exposure from electronic meters on residences, including single family homes and apartment complexes are within the FCC standards or are at levels to cause public health concern; and 2) to determine whether the current body of peer-reviewed literature has found an association between RF exposure from low level RF exposure and adverse health effects. ADHS reviewed available peer-reviewed literature to summarize potential health effects from radio frequency exposure, including exposure from electronic meters. ADHS also conducted a literature review of standards and guidelines for RF radiation used by a number of countries and health organizations and reviewed the personal anecdotes and journal articles submitted by concerned citizens. Finally, ADHS reviewed RF data collected from various meter types in Arizona to determine if the measured radio frequency is a public health concern.

From the information provided, it is painfully obvious that whatever funds expended by the Commission for this report, were a waste of both time and tax payer money.

As clearly stated, the goals of the requested report were

1) to determine whether RF exposure from microwave transmitting smart meters on residences, including single family homes and apartment complexes are within FCC standards or at levels to cause public health concerns

2) to determine whether the current body of peer-reviewed literature has found an association between RF exposure from low level RF exposure and adverse health affects.

While the ADHS did review **"select"** peer-reviewed literature, they cherry picked the data to coincide with their conclusions.

As clearly shown here, the data they chose to use (IEEE C95.1) is null and void, as it has not met the ANSI requirements for periodic reviews since 1999 (the date the information was last published.

Further, the study conducted by the ADHS does not even meet the ARRA standards for monitoring or measuring which also makes this report not worth the paper it is printed on.

The last sentence in this paragraph (pg 1; 3rd paragraph) states: "Finally, ADHS reviewed RF data collected from various meter types in Arizona to determine if the measured radio frequency is a public health concern."

The question arises as to exactly WHERE is the data collected? When was it collected? What was used to collect the data? Where is the copy of the current calibration sheets required by the ARRA posted? And how long were the tests run? None of which appears to be available to either the public or the Commission for review.

Does the Commission expect the public to accept a report based on conjecture and supposition? With the amount of time the ADHS has had, the report the ADHS submitted should be well over a thousand pages long, and filled with well documented findings of their research.

Background:

What is EMF/RF?

Electromagnetic field (EMF) radiation consists of waves of electric and magnetic energy moving together through space at the speed of light (FCC 2012). Radio waves and microwaves, emitted by transmitting antennas, are one form of electromagnetic radiation and are collectively referred to as "radiofrequency" or "RF" energy or radiation. The most important use for RF energy is in providing telecommunications services. Smart meters, cell phones, Wi-Fi routers, computers, and radio and television broadcasting are just a few of the many telecommunications applications of RF energy.

What they failed to define in the ADHS report, is that microwaves are a form of electromagnetic energy, like light waves or radio waves, and occupy a part of the electromagnetic spectrum of power, or energy.

Microwaves are very short waves of electromagnetic energy that travel at the speed of light (186,282 miles per second). In our modern technological age, microwaves are also used to relay long distance telephone signals, television programs, and computer information across the earth or to a satellite in space, or in this case to the utilities.

All wave energy changes polarity from positive to negative with each cycle of the wave. In microwaves, these polarity changes happen millions of times every second. As these microwaves are generated from the smart meter, they cause the polar molecules to rotate at the same frequency millions of times a second.

All this agitation creates molecular friction at the cellular level, which affects the health of the occupants within a home. The friction also causes substantial damage to the surrounding molecules, often tearing them apart or forcefully deforming them, causing physical harm to the occupants whether human or animal.

The scientific name for this deformation is "structural isomerism". Microwaves from smart meters produce a spiked wavelength of energy with all the power going into ***only one narrow frequency*** of the energy spectrum in a 360 radius since the meters do not possess a directional antenna.

Radiation, as defined by physics terminology, is "the electromagnetic waves emitted by the atoms and molecules of a radioactive substance as a result of nuclear decay." Radiation causes ionization, which is what occurs when a neutral atom gains or loses electrons.

In simpler terms, microwaves decay and change the molecular structure of soft tissue by the process of radiation. Had the manufacturers of the smart meter technology accurately called them "radiation meters", it's doubtful they would have ever been able to sell it to the public, but that's exactly what a smart meter is.

No FCC or officially released US government studies contrary to the Smart Grid Agenda (and Agenda 21) have proven current microwaving usage to be harmful, but we all know that the validity of studies can be - and are often times deliberately – limiting or completely devoid of accurate safe infomration .

> **How is radio frequency measured?**
>
> Radiofrequency has two components, an electric and magnetic component. A common unit for characterizing the total electromagnetic field is "power density," which is defined as power per unit area. It is commonly expressed in terms of watts per square meter (W/m^2) (FCC 2012). The quantity used to measure the rate at which RF energy is actually absorbed in a body is called the "Specific Absorption Rate" or "SAR," which is usually expressed in units of watts per kilogram (W/kg). In the case of exposure of the whole body, an adult absorbs RF energy at a maximum rate when the frequency of the RF radiation is approximately 70 MHz. Because of this "resonance phenomenon," RF safety standards are generally most restrictive in the frequency range of 30-300 MHz (FCC 2012).

First off, the true definition of a smart meter is that it is a **microwave** communication device operating in the 900+ Mhz frequency range that pulses up to 190,000 times a day not including a large scale data dump with a huge increase in output radiation for a short period occurring between 3 to 6 AM every morning, 24/7/365.

AMR or AMI is designed to monitor all electrical usage and end rush current for billing purposes. The meters are designed to make up for lost revenue from the lead and lag which was prevalent on analog meters. The end result is increased utility charges for all consumers. Also, none of the meters in use within Arizona are UL (Underwriters Laboratory) certified, making the fire danger and safety issues a grave concern to the public at large and a liability issue for the Commission.

How do electronic meters use radio frequency?

This report focuses on the usage of electronic meters. Electronic meters give utilities a means to match energy consumption with energy generation, and allow consumers to better manage their energy use. Four general types of meters are used in Arizona. The oldest meter type is analog, which displays energy usage on dials on the face of the meter. Power Line Carriers (PLCs) communicate with the electric company by using power lines, and do not use RF frequencies for communication. Automated Meter Reading (AMR) meters are one-way communicating meters that use RF frequencies to communicate usage data to the electric companies. Advanced Metering Infrastructure (AMI) meters are devices capable of two-way communication, and use RF frequencies for communication purposes. AMI meters send usage data to the electric company, and the electric companies can communicate with the meter, for example, starting and stopping service remotely.

Table 1. Metering technologies evaluated in this study

Type of Meter	Description	Frequency
Analog	The most common type of analog meter is essentially an electric induction motor that drives a series of geared wheels connected to indicators on the meter's face. The utility sends meter readers periodically to each meter, and no RF frequency is used.	N/A
Power Line Carrier (PLC)	Power-line communications usually operate by adding a modulated carrier signal to the existing home electrical wiring system. A PLC carries data on a conductor that is also used simultaneously for alternating current (AC) electric power	57-63 Hz

First off, the ADHS definition is grossly mis-stated here. These are NOT "electronic meters" in the pure sense of the definition as portrayed by the ADHS report. They are electronic electrical use surveillance devices with two way communication ability in the microwave band.

Early Generation I "electronic meters" in use by the utilities prior to 2008 were true electronic meters, and the only meters that meet this definition.

They monitored all electrical operation and use on a 24/7/365 basis. The only difference, was that they had to be read by meter readers using either a hand held device or by a drive by reader; as their broadcast capability was extremely limited to **direct polling only** from a close proximity location.

Neither APS nor SRP use PLC (Power Line Communication) devices to send and receive data at their billing facilities. While these are not only safer (and meet the ARRA requirements of alternative methods of reading data) they do not have the capacity to provide electronic and electrical surveillance on a consumer.

ADHS is also incorrect in stating that the AMR meters are "one way" communicating devices; but again they are referring ONLY to Generation I electronic devices. In order for any device to respond to a query, it has to answer a request.

AMI or "smart meters" are designed as "two way" microwave communicating devices which are the source and cause of all health related issues brought forth to the attention of the Commission and the ADHS.

Where the ADHS clearly states that AMI meters "are devices capable of two way communication, and use RF frequencies for communicating purposes. AMI meters send usage data to the electric company, and the electric companies can communicate with the meter, for example, starting and stopping service remotely. They are 100% incorrect in their belief that these meters use a "harmless" RF frequency to communicate. They do NOT use radiofrequency to communicate, they use pulsed microwave radiation to communicate.

As the attached graphs which the ADHS supplied clearly show, an analog meter (which has been in use for over 100 years) is **undeniably the safest meter on the market worldwide**. It produces NO RF frequencies within or outside the home, nor does it create any health hazards as the Smart Meters do.

Since neither APS nor SRP use PLC (power Line Communication) devices, this is a moot point.

AMR meters (or Generation I Electronic Meters) use a small low power microwave transmitter to send data **on demand only**. In essence they do communicate with two way communication, but are only active when polled for data and then only once a month for a very short duration – thus minimizing microwave exposure to near harmless levels.

AMI meters record ALL electrical usage 24/7/365 (in clear violation of state and federal wiretapping laws), then transmit (pulse transmissions) up to 190,000 times a day (24/7/365) with and huge meter data dump at extremely elevated microwave levels between the hours of 3 and 6 AM daily.

These meters also violate the easement allocation provided to the utilities for the installation of a "metering device", in that they have never been authorized by the consumer to install a microwave transmission device on their property, nor do they possess the proper clearances from the ARRA and the FCC to do so.. NO informed consent was given as NO honest information was provided by the utilities truthfully depicting these meters as microwave transmission devices was ever provided.

Since the only documentation provided by the utilities is that supplied by the EPRI (Electrical Power Research Institute) then this information cannot even be considered, as it is a clear conflict of interest, in that all the funding is provided solely by those with a vested interest in the AMI system.

None of these meters are UL (Underwriters Laboratory) tested although the UL has been trying to get them tested since their inception. Since the meters have gone from a straight electromechanical metering device of a simple design proven over a hundred years of service, AMI/AMR meters are run by electronics used to monitor the home or business, compute the data and then transmit it via microwave frequencies. Since none of these devices has any long term history, and have already been the subject of numerous lawsuits, fires and problems; then having them tested and registered by the UL only makes safe sense to protect the populace.

Most of the world has significantly lowered the acceptable standards for non-ionizing radiation based on their research and studies. The US is far behind the rest of the world in reaching the same conclusions, as the following graph clearly shows.

Both New Zealand and Russia has lowered the limits to protect their citizens from the non-ionizing radiation produced based on studies that are both up to date, and performed by those in the environmental medical fields.

The data set forth by IEEE is null and void, as it does not even meet their own standards of being reviewed and updated as required by law.

Table 2: Standards and Recommended Guidelines for 900 MHz Radio Frequency

Country/Organization	Standard/Guideline for Power Density	Citation
Federal Communications Commission (FCC, USA)	6 W/m^2 (Watts/square meter)	OET Bulletin 56: Fourth Edition, August 1999[1]
Australia	9 W/m^2	Radiation Protection Standard, May 2002[2]
Canada	4.5 W/m^2	Safety Code 6, 2009[3]
International Commission on Non-Ionizing Radiation Protection (ICNIRP)	4.5 W/m^2	ICNIRP Guidelines for Limiting Exposure..., 1998[4]
Institute of Electrical and Electronics Engineers (IEEE)	4.5 W/m^2	IEEE Exposure Limits..., 2005[5]
New Zealand	0.5 W/m^2	Radiofrequency Fields Exposure Standard, Feb. 2014[6]
Russia	0.1 W/m^2	Scientific basis for Soviet and Russian Radiofrequency Standards..., July 2012[7]

Links: [1]FCC [2]Australia [3]Canada [4]ICNIRP [5]IEEE [6]New Zealand [7]Russia

This study reviewed a number of studies on animals, including rats and rabbits. It was found from this animal data that exposure to more intense fields, producing Specific Absorption Rate (SAR) values in excess of 4 W/kg, can overwhelm the thermoregulatory capacity of the body and produce harmful levels of tissue heating. The sensitivity of various types of tissue to thermal damage varies widely, but the threshold for irreversible effects in even the most sensitive tissues is greater than 4 W/kg under normal environmental conditions. These data form the basis for an occupational exposure restriction of 0.4 W/kg and a community exposure restriction of 0.08 W/kg, which provide a large margin of safety for other limiting conditions such as high ambient temperature, humidity, or level of physical activity (ICNIRP 1998). These values can then be converted from SAR to their equivalent power density.

Isn't it ironic that the Russian study concluded that the potential for harm and damage to humans was far greater than originally claimed by either the IEEE or the FCC. Further, isn't it sad that the data the ADHS chose to use is both inaccurate and out of date by their own standards?

The Institute of Electrical and Electronics Engineers (IEEE):

The Institute of Electrical and Electronics Engineers (IEEE) is a professional association, whose objectives are the educational and technical advancement of electrical and electronic engineering, telecommunications, computer engineering, and allied disciplines. The guideline determined by IEEE has a similar rational to that of ICNIRP, but was developed using different processes. Based on its review, IEEE concluded that disruption of food-motivated learned behavior in laboratory animals is the most sensitive biological response that is both well confirmed and predictive of hazard. This effect, known as behavioral disruption, has been observed in laboratory animals ranging from rodents to monkeys exposed to RF fields at frequencies ranging from 225 MHz to 5.8 GHz. Depending on the animal species and RF frequency, the exposure needed to produce behavioral disruption varied from 3.2 to 8 W/kg (Ziskin 2005).

From its literature review, IEEE chose a value of 4 W/kg for the whole body averaged SAR as the threshold for behavioral disruption in animals. It reduced this SAR by a factor of 10 to establish the basic restriction for exposure in controlled environments, and then added another factor of 5 for exposure in uncontrolled environments. The resulting basic restrictions on whole body SAR are 0.4 W/kg for controlled environments, and 0.08 W/kg for uncontrolled environments. These values can then be converted from SAR to their equivalent power density. For 900 MHz radio frequency, the equivalent power density is 4.5 W/m^2.

As clearly stated and shown, the data used is flawed and inaccurate by the IEEE's own standards as found in section 6, titled "Rationale" where is clearly states that "***American National Standards Institute (ANSI) policy requires that each of its standards or guides be reviewed at 5-year intervals***." In checking the only date associated with the IEEE C95.1-1999 report it clearly shows that it is dated 1999, with no listing of any revisions having been made to it since that date. Based on that information, then the IEEE report is in direct violation of its own acceptable standards, and therefore null and void as acceptable data for consideration.

Russia:

Radiofrequency (RF) standards for both public and occupational health issued by the Russian Federation have always contained exposure limits that were below those in other countries. Their guideline of 0.1 W/m^2 was based on the study: Vinogradov GI, Naumenko GM, Vinarskaya EM, Gonchar NM. 1987. Biological significance of autoimmune reactions of the organism after exposure to environmental factors. Gig Sanit 1:55-58 (in Russian).

This study reviewed a number of studies on animals, including rabbits, guinea pigs, white rats, wistar rats, and female fisher rats. Based on the immunology studies discussed in the article, chronic daily exposure to 1-5 W/m^2 can induce persistent pathological reactions. The threshold exposure for the unfavorable biological effects (0.5 W/m^2) was found in the immunology studies, but these effects were not pathological since the organisms could compensate for the exposure. The authors concluded, however, continual compensation could lead to long-term adverse effects and thus should be protected against. Chronic exposure to 0.1-0.2 W/m^2 did not induce any noticeable biological changes in small laboratory animals. Therefore the guideline in Russia is 0.1 W/m^2.

The conclusion drawn by the Environmental Medical Experts clearly state one undeniable fact: **"The authors concluded, however, continual compensation could lead to long-term adverse effects and thus should be protected against."** They chose to set their limit to a low standard to protect their people – unlike the ADHS whose report supports utility standards and rhetoric.

Since there is NO long term studies that have been performed on any of the smart meters made – nor has any long term effects been studied in the utilities bid to install these without safeguards, then shouldn't every institute within the country be erring on the side of caution as Russia has to protect their people?

As to the four states the ADHS has chosen to quote, all of them have based their conclusions on the same flawed data, citing the IEEE standards. Since these have been clearly shown to be in violation of their own standards, then these reports are also null and void and based on out of date information and cannot be considered.

Under the heading of Scientific Studies the ADHS states:

Review Articles

ADHS performed a literature review of the potential health effects caused by exposure to RF radiation. ADHS searched two different literature databases of peer-reviewed articles. ADHS searched for review articles and articles that discussed an association between RF exposure and any of the top five health concerns from community members (see below). Preference was given to review articles that 1) discussed radiation from electronic meters, and 2) were published within the last 5 years if they could be found.

This appears to be the first mis-step by the ADHS, in that they have inadvertently clearly described the pulsed microwave non-ionizing radiation correctly.

ADHS found that most experts agree that exposure to RF at high enough strengths for long enough time can result in adverse health outcomes from thermal effects. However, when discussing non-thermal adverse health outcomes, the literature is not clear.

How is it that the ADHS clearly admits that " most experts agree that exposure to RF (microwave) at high enough strengths for long enough time can result in adverse health outcomes from thermal effects"; yet came to the conclusion that these meters are safe? They go on to also clearly state: "However, when discussing non-thermal adverse health outcomes" that the literature is not clear.

Wouldn't that scream to the ADHS that there is not sufficient data to either prove or disprove their conclusion at this time? If that is the case, then why did they choose to side with the utilities instead of sound medical practice of erring on the side of caution?

Other literature ADHS reviewed discussed potential changes on the cellular level which provide knowledge of the basic interaction mechanisms of RF with cellular structures. These studies are important hypotheses generating studies. They provide evidence that RF may have the potential to affect human physiology. However, these studies cannot conclude that the cellular changes necessarily lead to disease. Other studies concluded exposure to RF from a variety of sources was associated with adverse health outcomes. However, these studies had several limitations ranging from recall bias to a lack of details, e.g. power densities of exposure or differentiating between exposure to electronic meters and other types of RF emitting devices. Sometimes a study that suggests an exposure is associated with an adverse health outcome is countered by another similar study that suggests there is no adverse health outcome at that exposure level.

Again, their report clearly states that the studies they perused showed that there is evidence (key word here) that RF (microwave) may have the potential to affect human physiology", then in the very next sentence state "however, these studies cannot conclude that the cellular changes necessarily lead to disease."

As previously stated, since none of these meters have had any long term studies performed on them, then it is clear that the data available is insufficient at this time to draw ANY SAFE conclusions.

When even the UL is stating they need to be tested, then someone ought to stand up and take notice. The UL does not jump into anything they do not feel represents a potential hazard to the populace.

The paragraph goes on to state "Other studies concluded exposure to RF from a variety of sources was associated with adverse health outcomes." Since the only source in question here is the microwave radiation from smart meters, then the ADHS should have honored their mission statement and erred on the side of caution.

> ADHS considered articles' study design, exposure parameters, and relevance to this current review. The study design and exposure parameters vary widely from study to study. ADHS attempted to concentrate on those studies that addressed the questions relating to community exposure to RF from electronic meters.

Again, it is apparent that the ADHS does not understand nor is capable of making the distinction between an electronic meter and a smart meter. That simple observation alone is enough to throw out their findings. If one cannot make the distinction, then how can they accurately conclude they are not a threat?

> It is generally well understood that RF exposure can cause tissue heating or "thermal effects," leading to potential adverse health effects. More recently, concern has been raised that exposure to lower power densities of RF may lead to adverse health effects without tissue heating, also known as "non-thermal effects." Several studies in the last decade have concluded that RF exposure at lower power densities than those required to cause thermal effects may cause adverse health effects including genotoxicity, decreased sperm count, headaches, sleep problems, concentration problems, and hyperactivity in children. The studies that draw these conclusions are largely based on exposure to cell phones and Wi-Fi devices held close to the human body such as a laptop on a man's lap leading to decreased sperm quality/count. In addition, many of these conclusions were based on results that showed biologic changes. Biologic changes do not always lead to the expected adverse health outcome. The National Aeronautics and Space Administration (NASA) describes the difference of biologic and adverse effects as follows:

Once again, the defense is to always fall back on cell phones and wi-fi. The argument is flawed in that exposure to either of these devices is:

1) By choice
2) Limited
3) And can be switched off

Smart meters radiate 24/7/365, and pulse up to 190,000 times a day. Also what is never discussed is the "data dump" they perform in the early morning hours to the utilities. Since these cannot be

switched off and every home overlaps the other creating an overlapping field of microwave radiation, then the accumulation of the radiation is increased proportionally to levels not discussed.

"Biological effect — A biological effect is an established effect caused by, or in response to, exposure to a biological, chemical, or physical agent, including electromagnetic energy. Biological effects are alterations of the structure, metabolism, or functions of a whole organism, its organs, tissues, and cells. Biological effects can occur without harming health and can be beneficial. Biological effects also can include sensation phenomena and adaptive responses.

Adverse health effect — A biological effect characterized by a harmful change in health." (NASA, 2014)

"Biological effect — A biological effect is an established effect caused by, or in response to, exposure to a biological, chemical, or physical agent, including electromagnetic energy. Biological effects are alterations of the structure, metabolism, or functions of a whole organism, its organs, tissues, and cells. Biological effects can occur without harming health and can be beneficial. Biological effects also can include sensation phenomena and adaptive responses.

Adverse health effect — A biological effect characterized by a harmful change in health." (NASA, 2014)

Since ADHS chose to quote the NASA definitions, how did they miss where it states that "biological effects are alterations of the structure, metabolism, or functions of a whole organism, its organs, tissues, and cells?"

Exactly WHAT has been reported by Environmental Medicine Groups around the world? Are not their reports clear that the non-ionizing radiation produced by smart meters create alterations to the structure, metabolism and functions of the whole organism? Do not the list of adverse health effects being experienced and documented clearly show adverse affects to organs, tissues and cells. Does not NASA clearly state (in 2014) that an adverse health effect is characterized by a harmful change in health?

Is it the ADHS contention that all the effects being experienced and documented by people across the globe is "in their heads"?

For example Juutilainen, et. al. reviewed *in vitro, in vivo,* and human studies on a variety of adverse health outcomes. The authors stated, "the studies discussed in this review indicate that there may be specific effects from amplitude-modulated RF electromagnetic fields on the human central nervous system. The effects reported (changes in EEG, cerebral blood flow and performance in a memory test) are relatively minor, and do not at present allow conclusions concerning possible adverse health effects." They went on to say:

> "Further studies are warranted to determine how the effects depend on modulation characteristics and exposure level, and to investigate possible mechanisms and relevance to human health. Also, animal studies with suitable experimental models would be valuable to shed light on the mechanisms of the modulation-dependent effects on the central nervous system.
>
> No consistent evidence has been found for modulation-dependent effects on carcinogenesis or genotoxicity. Some in vitro studies have provided suggestive evidence of modulation-specific effects at the cellular level. Follow-up of the positive findings would be helpful for understanding the mechanisms of any specific effects of modulated RF energy."

Since literally everything the ADHS has quoted clearly state that further studies are warranted to determine the long term effects then how can they draw a conclusion that smart meters pose no risk? Common sense alone clearly shows that these meters have not been around long enough to determine the dangers they pose, yet the ADHS believes they are better educated and informed than the rest of the worlds own Environmental Medical Experts.

It is also apparent the the ADHS chose to pick and choose exactly what they included in their report yet numerous key factors stand out that even they could not hide or deny, such as:

> Whether a person experiences an adverse health outcome from RF depends on many factors. Factors include how strong the power density is, how far the person is from the RF field, how often the person is exposed, and the individual health of the person exposed.

Under the heading of "Individual Health Effects" the ADHs stated the following:

The articles ADHS found discussed RF from sources other than electronic meters. A number of the articles discussed the potential health effects listed above from RF radiation emitted from cell phones. Electronic meters use a very similar wireless technology to cell phones, and the electronic meters in Arizona use a frequency of 900-930 MHz, which is within the frequency range of cell phones (450-2700 MHz). However, strength of the RF field and exposure to electronic meters and cell phones differ.

Most of the studies concluded that there was no association between RF exposure at low levels and adverse health outcomes. A couple of articles found weak associations. Some studies called for additional research (Mohler, 2012; Lowden 2011; Heinrich 2010; Mortazavi 2014; Poulsen 2013; Swerdlow 2011; Kwon 2012; Choi 2014; and Frei 2012).

Once again, the ADHS chooses to misidentify a smart meter as a "electronic meter"! As previously stated, if they are incapable of making the clear distinction, between an electronic meter and a smart meter, then any conclusion drawn would be incompetent and fraudulent.

There is absolutely NO similarity between cell phone wireless technology and a smart meter. One uses RF technology the other uses microwave technology. If the ADHS cannot make the distinction then again, the validity of their report comes into question.

Smart meters broadcast in the 900-930 Mhz range which according to their own report clearly puts them in the middle of microwave transmission spectrum, NOT the radio frequency spectrum.

Where the ADHS state that "most" studies conclude that there is NO association between RF exposure at low levels and adverse health outcomes, earlier in this rebuttal they clearly stated that there are associations with microwave radiation and adverse health effects. So which is it?

They go on to state that "a couple" (really) of articles find "weak association; and "some" call for additional research!

The fact is MOST call for additional research and almost ALL clearly state there is insufficient data to draw a safe conclusion. SO is the ADHS deliberately lying to the people of Arizona and the Commission, or are they just incapable or unwilling to state the truth?

Under the heading of "FIELD STUDY"

ADHS worked with ARRA to design a field sampling plan that would measure different meter technologies in urban and rural areas. The agencies used their expertise and referred to previous studies to identify a scientifically sound method. The agencies approached the field study by attempting to capture a worst case scenario as a screening process. If a measurement was captured at or above the screening value, a more in depth evaluation would be necessary. The field study was not intended to strictly follow FCC's recommendations for evaluating human exposures to RF, but rather capture the worst case scenario. The FCC guidelines consider percent Maximum Permissible Exposure (MPE) and duty cycle when comparing the measured RF exposure to the standard. This study measured peak and average power densities at 5, 10, and 15 minutes without regard to duty cycle.

Let's break this down as stated above:

1) The ADHS worked with the ARRA to design a "field sampling plan"
2) Where is the plan documented?
3) "The agencies used their expertise and referred to previous studies to identify a scientifically sound method." What was the method and where is it documented?
4) "The agencies approached the field study by attempting to capture a worst case scenario as a screening process." How could this have been accomplished within the time allotted at 5, 10 and 15 minute intervals?
5) "The FCC guidelines consider percent Maximum Permissible Exposure (MPE) and duty cycle when comparing the measured RF exposure to the standard." Since we have already proven that the standards they use are null and void, then the entire test is null and void by the very standards set forth by the IEEE and FCC.
6) MPE is a time weighted average, which clearly means it is taken over a long period of time over several days, weeks or months – NOT minutes.
7) "The study measured peak and average power densities at 5, 10 and 15 minutes without regard to duty cycle. You HAVE to take into account the duty cycles since these meters pulse up to 190,000 times a day! You cannot come to a conclusion based on insufficient data within a micro-allotted timeframe.
8) Exactly WHO conducted the measurements, what was his background: where is the logged data published; where is the documented calibration sheets required by the ARRA available for public dissemination?

It was decided that ARRA would test the RF emitted from a variety of meter technologies: analog, PLC, AMR and AMI. The Arizona Radiation Regulatory Agency (ARRA) conducted the field sampling analyzed in this report. ADHS used the measured RF levels to determine if there is a public health concern associated with exposures to electronic meters in Arizona. Sampling was conducted from June to September 2014 by ARRA. Only outdoor sampling was conducted at residential locations for single-family homes and apartment complexes.

The ADHS states that ARRA tested the "RF emitted from a variety of meter technologies: analog, PLC, AMR and AMI."

Since the ARRA conducted the sampling, where is their report? Why is it not included in the ADHS conclusions?

Why was "only outdoor sampling conducted"? Why not from within the structures where people are complaining about the effects of the meters? How did the ARRA conclude that there was NO health concerns and where is their data?

Radiofrequency Sampling Device

The Tenmars TM-195 is a radio frequency (RF) field strength meter. It is designed for measuring and monitoring RF electromagnetic field strength over the frequency range of 50 megahertz through 3.5 gigahertz. This meter self-calibrates at power up levels but has a functionality to be manually adjusted to detect more sensitive frequencies inside of multiple frequency fields. Field strength meters will display excessive values if hand-held or moved during measurements from electrostatic charges. To counter this, the TM-195 should be used on a tripod or held as steady as possible while avoiding speaking or moving during measurements. The electrical specifications are as follows:

With all the available equipment out there for use, why would the ARRA and the ADHS choose to use a sub-standard meter that does not have the capability to record and track data? The Tenmars TM-195 is a baseline meter that provides questionable readings when compared to meters those specifically designed to monitor, track, and document the readings they produce.

According to the ARRA, ALL their measuring devices are supposed to be calibrated and verified on an annual basis. Where is the documentation showing the last time the meter was calibrated? Self calibration on any device which can be changed for sensitivity on the field is NO calibration for precision measuring. Therefore since none of this information is present, the report should be considered null and void as are the conclusions drawn.

The Arizona Radiation Regulatory Agency uses this meter during routine use to ensure that industrial registrants registered to operate radio frequency devices do not exceed the maximum permissible exposure (MPE) limits as defined in the Arizona Administrative Code Title 12, Chapter 1, Article 14. Calculations of the MPE are published in IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz.

How can the ARRA use a meter that does not meet their standard for measuring? The fact that they are using the cheapest meter on the market and one that does not provide recordable data is worrisome at least and dangerous at best.

Since it has already been proven that any reference to IEEE standards are not viable, then all the data based on it is null and void. The required IEEE standard are 16 years past the required updates by law, and their own standards.

Trial Sampling Event

A trial sampling event was conducted at a residential, single-family home and an apartment complex to determine the feasibility of various sampling parameters. At this event, two distances (three feet and nine feet), use of attenuation and no attenuation, and time intervals (readings every 15 minutes for one hour) were considered. It was determined that spending one hour at each location would significantly limit the number of total sampling locations in the final review. In order to 1) sample more locations, 2) measure the same location multiple times at different times of the day, and 3) sample locations across the state, it was decided to adjust the sampling parameters to measure the maximum radiofrequency a person may be exposed to from the electric meter, the worst-case scenario.

Pulse modulated vs. continuous-wave (CW) RF radiation

Many other studies provide evidence that nonthermal modulated-RF exposures produce effects that are not produced by CW (unmodulated) RF radiation. Meaningful studies of biological and health effects of nonthermal, pulse-modulated RF radiation exist including studies that sghow injury to the eye (Kues et al., John Hopkins Applied Physics Laboratory (JHAPL). The significance of thee results, even at the early stages of this continuing research, was responsible for the development and adoption of an RF radiation exposure standard by JHAPL (in 1984) for their personnel. The JHAPL MPE for frequencies from 30 MHz to 100 GHz is 0.1 mW/cm2. This standard provided the basis for the 0.1 mW/cm2 action level used to protect personnel from harm from RF radiation generating equipment at the Hughes Aircraft Company. The JHAPL MPE is a factor of 100 times more stringent than the 1992 ANSI/IEEE MPE for controlled environments for the frequency range of 3.0 GHz and above.

Pulse modulated RF radiation can produce a response that is called "microwave hearing". This effect seems well established and probably results from very rapid thermoelastic expansion of the brain, creating a sound wave in the head. Conditions under which the auditory effect can be invoked in people with normal hearing should be avoided according to the National Radiological Protection board (NRPB) draft recommendations for workers and the public. In contrast to this recommendation, the 1992 ANSI/IEEE standard states that the human auditory effect is clearly not deleterious; it recommends a limit for pulsed radiation that is well above the threshold for auditory effect.

Trial sampling was stated as being done at 3 feet and 9 feet over the course of one hour. Which hour? What time? Where is the documentation? Since MPE can only be determined by a time weighted average, then how can any conclusions be drawn in an hour?

Please answer the following questions:

1) How many pulses were noted within the hour at these locations?\
2) How frequently were the logged?
3) What locations were re-measured and at what time of the day or night?
4) Did the density of the readings change at the differing locations?
5) Was any measurements taken during their routine data dumps?
6) What was the measurements then

7) Did the pulsing ever subsist during their hour survey.

How can this report (if you can call it that) be considered accurate by any precision measuring standard? The ADHS states "In order to 1) sample more locations, 2) measure the same location multiple times at different times of the day, and 3) sample locations across the state, it was decided to adjust the sampling parameters to measure the maximum radiofrequency a person may be exposed to from the electric meter, the worst case scenario."

1) First off, where is it documented insofar as the parameter changes?
2) Exactly WHAT were the parameters?
3) Measurement would be for non-ionizing microwave transmission NOT radiofrequencies.
4) The purpose of the report was to measure the output of Smart Meters, NOT Electric meters.
5) How can a worst case scenario be measured when you are looking at a true time weighted average of differing locations over a long period of time both inside and outside a location?
6) Since the ill effects are based on a cumulative basis, then anything less than a true time weighted average of hours, days, weeks and months can only be considered as relevant.
7) Where are the graphs and charts showing the attenuation (peaks and valleys) of the pulse shown?
8) How was the documentation stored and verified? Was it written down? Does the commission have logs and graphs showing the findings? If not, why not?

Results and discussion

On-site Readings of Radio Frequency Electromagnetic Fields

The RF electromagnetic field emissions associated with the usage of electronic, PLC, and analog meters were measured by using a RF field strength meter, Tenmars TM-195, as described in the Methods section. This field investigation examined the strengths (measured by power density in watts per square meter, W/m^2) of the RF fields emitted by different types of meters under normal operating conditions because the electric companies were not notified when the investigation was conducted. This was determined by the study group (i.e. ACC, ARRA, and ADHS) to prevent bias.

The non-ionizing microwave RF radiation emissions for all meter types are suspect at best when compared to a real time weighted average based over established time periods without interruption. As previously stated,

1) Nowhere is the calibration documentation presented or provided;
2) Nowhere are the individual who made the survey credentials presented;
3) Nowhere is there detailed data logging that can be reviewed;
4) Nowhere has the ARRA provided a copy of the permits required by law for operation of any non-ionizing device by any entity;
5) Nowhere has the ARRA posted the individual permits required by law for each facility (home, apartment, business, etc.);
6) Nowhere has the ARRA or the ADHS provided fact based conclusion based on accurate available standards or information.

The amount of transmitting activity of an electronic meter varies throughout the day. It depends on the prescribed data-collecting times and the interaction with other meters. In addition, the typical emission of an electronic meter consists of very brief spurts of pulses of RF energy lasting less than one-tenth of a second. To represent the overall exposure throughout a day, power density measurements were taken at three different times during the day (for example, morning, midday, and afternoon) for each sampling location. Both the average and instant peak values of field power density were measured. The measurements were taken at 1 foot away from the meter without attenuation. The measurements represented the maximum RF emission a person (i.e. worst case scenario) can be exposed to from the meters at the sampling time.

Definition - What does Time-Weighted Average (TWA) mean?

Time-weighted average (TWA) is a measure of a human's average exposure to airborne and other harmful contaminants as well as hazards such as noise or radioactivity. TWA is usually calculated over a period of eight hours, or the typical work day.

1) How much does it vary throughout the day
2) How does the interaction between meters come into play – why is it not explained or detailed
3) How many pulses are emitted throughout the day?
4) How many within an hour?
5) One-tenth of a second continually still presents a significant cumulative effect not documented here.
6) Measurements taken at intervals do NOT produce an accurate Time Weighted Average of MPE when large blocks of time are missing from the data stream.
7) Again, where is the documentation?
8) How was it stored?
9) The measurements do not project an accurate or reliable level of exposure when looked at in a Time Weighted Average for MPE, as this was not performed
10) The Tenmars TM-195 does not provide the level of precision to determine the overall ill health effects that are being reported.
11) Since these meters operate 24/7/365, then the minimum TWA should be 24 hours since that is the maximum amount of exposure or in this case the "worst case scenario".

ADHS compared the levels of RF power density measured in front of different types of meters (Table 3). As expected the measured RF levels are higher for AMI and AMR meters because they communicate via radio frequency. ADHS compared the levels of RF power density measured in front of single and multiple meters (Table 4.) As expected the measured RF levels are higher for multiple meters. ADHS also compared the levels of RF power density measured at urban and rural areas (Table 5.) Overall, the RF levels are higher in urban area. These results indicated that, under the sampling scenario, people will receive higher levels of RF exposure from multiple meters. Yet, as discussed later, none of the measured RF power density are at levels of public health concern.

1) Where is the documentation and the readings for those complexes that the ADHS clearly admits are "higher" for multiple meters?
2) Exactly how high were they?
3) Where are they distinctly labeled in their report?
4) What effect do these amount of meters have on the health of the occupants?
5) Where are the readings for "urban" areas and at what levels were they?
6) How were they measured?

With all the data that the ADHS has used, and all the questions that have arisen base don the information provided; exactly HOW can the ADHS assume that none of the power density levels measured are of concern or health risks to the public?

Public Health Implication Based on the On-site Readings

ADHS generally follows a three-step methodology to assess public health issues related to environmental exposures. First, ADHS obtains representative environmental data for the site of concern and compiles a comprehensive list of site-related contaminants or concerns. Second, ADHS identifies exposure pathways, and then uses standards or guidelines to find those exposures that do not have a realistic possibility of causing adverse health effects. For the remaining exposures, ADHS reviews recent scientific studies to determine if exposures are sufficient to impact public health.

This statement is by and large the most incompetent of the entire report based on the following:

1) ADHS states that it follows a 3 step "methodology" to assess public health issues which are:
   a) They "obtain representative environmental data for the site of concern and compiles a comprehensive list of site-related contaminants or concerns" Where is this at?
   b) They identify "exposure pathways and then use standards or guidelines to find those exposures that do not have a realistic possibility of causing adverse health effects." Exactly WHAT are the identified exposure pathways they identified? What standards are they using?
   c) They "review" recent scientific studies to determine if exposures are sufficient to impact public health" There are literally thousands of scientific reports clearly stating that these meters are not safe! Did the ADHS choose not to include those reports or findings? Lets take a look later in this report.

ANSI has adopted C95.1-1992, a revision of the 1982 standard, and the FCC has proposed its adoption. The new standard "contains a number of significant differences from guidelines and recommendations issued by ANSI in 1982. In many respects, the 1992 guidelines are more restrictive in the amount of environmental RF exposure permitted, and they also extend the frequency range under consideration to include wireless frequencies. The new 1992 guidelines specify two sets of exposure recommendations, one for 'controlled environments' (usually involving workers) and another for 'uncontrolled environments' (usually involving the general public). (FCC 93-142). These power densities are typically measured in units of "milliwatts per square centimeter", or "mW/cm2". For a typical cellular frequency, the proposed standard is 2.96 mW/cm2 for controlled environments and 0.592 mW/cm2 for uncontrolled environments. These standards have been set at levels which are a factor of 50 below the level where possible hazardous effects have been observed. For the purposes of comparison, a typical UHF television station broadcast antenna delivers a power-density of about 0.010 mW/cm2, compared to the applicable ANSI standard of 0.37 mW/cm2.

These on-site readings were compared to standards and guidelines, which are often used as screening tools to evaluate environmental data relevant to exposure pathways. The standards and guidelines are quite conservative, and include safety factors that account for sensitive populations (such as infants, young children, and elderly.) Adverse health effects are not expected to occur if an exposure level is below a health-based guideline. However, an exposure level at or above the health-based guideline does not mean adverse effects will occur. Rather, it means that there is a need to conduct a site-specific exposure scenario evaluation. The health risk for an individual depends on individual human factors (e.g. personal habits, occupation, and/or overall health), and site-specific environmental exposure factors (e.g. duration and amount of exposure). Therefore, the health-based guidelines should not be used to predict the occurrence of adverse health effects without looking at site-specific conditions.

Since the "standards and guidelines they continually quote are based on outdated and non-acceptable data, then the "conservative standards and guidelines" so-called safety factor cannot be considered as safe.

How can the ADHS draw the conclusion that "an exposure level at or above the health-based guideline does not mean adverse effects will occur?

Since the ADHS chooses to use a double standard here, lets break it down:

1) "The health risk for an individual depends on individual human factors (e.g. personal habits, occupation, and/or overall health) Everything listed cannot be considered, when smart meters know no limits, are not a choice, does not matter about occupation or health. Smart meters operate 24/7/365 with no concern for anything the ADHS lists
2) Site specific exposure factors? Every home and apartment, business or structure requiring electricity then becomes "site specific. Overlapping radiation levels from each home then comes into play not only outside the home but within the home.
3) Duration of exposure? What choice does anyone have who lives in a structure with a smart meter? Do they not live, sleep, eat, and play? Do they not raise children there?
4) How can any logical mind make the statement "therefore, the health-based guidelines should not be used to predict the occurrence of adverse health effects?" Exposure to non-ionizing radiation is a cumulative effect over a long period of time – it does not happen once in a while – it is happening 24/7365 without a break.
5) The conclusion drawn here appears to be one of bias and predetermined outcome. It is NOT fact based, it is not clinically based and it definitely is not based on extracted and established empirical data

ADHS typically uses standards and guidelines as follows: if an exposure is never found at levels greater than its standard or guideline, ADHS concludes the levels of corresponding exposure do not pose a risk to human health. If, however, an exposure is found at levels that are greater than its standard or guideline, ADHS examines potential human exposures in greater detail.

How can the ADHS determine if an exposure is not found at levels greater than its standard or guideline that it poses no risk to human health? Any doctor or scientist worth his salt would clearly

admit that a one time exposure is not a factor! However, even a high school student studying science knows about cumulative effects!

It is obvious that although the ADHS states that if "exposure is found at levels greater than its standard or guideline that they examine potential human exposures in greater detail; that it has little or no desire to do this. Samples taken at predetermined times over short periods do not provide even a close picture of the overall cumulative effects that cause ill health effects for anyone.

At best this report is totally incompetent, at best it was done with total disregard fot the health and safety of the people of Arizona.

Meters communicate via radio frequency (i.e. AMI and AMR meters):
Measured power densities were compared to health-based guidelines (Table 6.) The 30-minute averages were calculated by using the top six 5-minute averages from a sampling location. This approach provided an estimation of the possible maximum 30-minute exposure throughout a day. The overall averages were calculated by using all 5-minute averages from a sampling location. This provided an estimation of the overall exposure throughout a day. ADHS used guidelines developed by FCC, ICNIRP, IEEE and Russia to evaluate the potential adverse health effects associated with exposures to radio frequency from AMI and AMR meters.

By their own report, they base their findings on an "estimation" not fact!

No one, anywhere in the industry would attempt to extrapolate something as critical as cumulative exposure based on limited data and supposition.

Only a true Time Weighted Average over a long haul will provide the details needed to make an informed decision. This is nothing short of criminal, and puts the state, the Commission and the people at great risk.

Short-term Exposure: FCC, ICNIRP and IEEE guideline values was determined based on established adverse thermal health effects. The purpose of these guidelines are to prevent whole-body heat stress and excessive localized tissue heating. The 30-minute averages ranged from 0.000021 to 0.000465 W/m^2 for AMR meters, and from 0.000028 to 0.001101 W/m^2 for AMI meters. None of these values exceeded the FCC (6 W/m^2), or ICNIRP/IEEE (4.5 W/m^2) guideline values (Table 6.)

Since the standards are null and void, then the report is of no consequence. Since this is not a TWA to determine MPE, then any conclusions drawn are moot.

Long-term Exposure: FCC does not have an established standard for non-thermal health effects because of insufficient information. Our review of US and most internal government assessments, and scientific publications indicated that there is no consistent or convincing evidence to support a cause-and-effect relationship related to the exposure to the RF frequency (900 – 930 MHz) used by the smart meters. The majority of the scientific studies concentrated on the possible health effects from mobile phone exposure. When compared to mobile phones, smart meters represent lower RF exposure sources because of the attenuation factor of the building structure (for example: walls), and the distance from radiation signal source (i.e. location of the smart meters and mobile phones in relation to the human body.) Based on these, it appears to us that exposures to smart meters would indicate even less association to non-thermal effects.

Their first sentence says it all and is the only thing of credibility: Long term exposure: FCC (which relies on IEEE C95.1-1999) does **NOT** have an established standard for non-thermal health effects because of **INSUFFICIENT INFORMATION."**

Another flaw in their assumption and conclusion is based on the simple fact that they state "when compared to mobile phones, smart meters represent lower RF exposure sources because of the attenuation factor of the building structure (for example walls) , and the distance from the radiation signal source.

It is apparent that the "doctors" have absolutely NO knowledge of microwave operation. First off mobile phones can be switched off – smart meters cannot. Secondly the copper wiring and related metal within the home act as an additional antenna causing internal radiation from electrical wiring throughout the home. Since there is overlapping radiation within the smart grid – the radiation levels are constant and varying as each meter pulses continually through walls, windows and ceilings repeater towers.

Our review indicated that Russia has developed a standard for radio frequency between 450 to 2,700 MHz for mobile phones. This standard was determined based on non-thermal health effects. We do not have access and do not have the ability to review the original paper (in Russian). The source indicated that this value was set based on an animal study consisting of 110 rats exposed to 900 and 1,800 MHz at 5 and 20 W/m^2. The results showed changes in the immune status of animals exposed to 5 W/m^2. A safety factor was applied to obtain the Russian standard of 0.1 W/m^2 for the general public. This limit was set to ensure that no exposure would cause any possible biological consequences among the exposed population. ADHS used the Russian standard as a comparison to ARRA's measurements. The results showed that none of the overall average readings of AMI (ranging from 0.000025 to 0.000888 W/m^2) or AMR (ranged from 0.000016 to 0.000377 W/m^2) meters exceeded the standard (Table 6.)

Ironically the ADHS had the audacity to make this statement: "The limit was set to ensure that no exposure would cause any possible biological consequences among the exposed population."

Since none of the data that the ADHS has used qualifies as accurate or reliable, then how can they violate the very mission statement indicated below?

The Arizona Department of Health Services ***promotes and protects the health of Arizona's children and adults.*** Its mission is to set the standard for personal and community health through direct care, science, public policy, and leadership.

From the very basis of their mission statement which claims that the ADHS is to set the standard for personal and community health through direct care, science, public policy and leadership; then how come they did not do their due diligence in assuring that the data they used was both reliable and current?

Since the ADHS has chosen to use the Russian limits (as well they should) then it is in their best interest to perform a study that exceeds minimal effort and reliability.

> In this field investigation, ARRA measured the RF emission levels based on the worst case scenario. Such measurements do not necessarily reflect personal RF exposure (they tend to overestimate the RF exposures) because they are not always taken at the distance from the RF source that the person would typically be from the source (for example: inside the house) Therefore, with the available information, exposures to AMI and AMR meters are not likely to harm the health of the public.

This paragraph is by and large the single most incompetent statement and assumption made by the ADHS. The readings taken do NOT accurately reflect a "worst case scenario", as they are not a Time Weighted Average, but a minute sampling of varying locations (at best) at specific times of day within a test area.

Personal exposure limits cannot be calculated based on supposition and guesswork! All limits are checked over long periods and reading are not just taken within guessed boundaries. Any test of an area must be performed using proper equipment designed to document and log ALL parameters on a continual basis, provide a second by second, minute by minute, hour by hour, day by day, week by week analysis to determine if the exact Maximum Permissible Exposure Limits have been reached or exceeded.

Anyone who has performed safety evaluations knows this to be true. What was performed by the ADHS and ARRA is nothing short of criminal in its findings and unsafe in its conclusions. How can the ADHS make the comment that exposure tends to be overestimated for microwave exposure when by their own admission they did not do their due diligence in monitoring the reading from within a home?

By their own admission, they acknowledge that that their information is incomplete and does not reflect the data required to make an informed decision, yet they announce the following: "Therefore, with the available information, exposures to AMI and AMR meters are not likely to harm the health of the public."

Conclusions

Review of Radio Frequency Regulation and Literature:

ADHS reviewed: (1) regulatory standards developed by the US and other countries such as Australia, Canada, Russia, and New Zealand, (2) exposure recommendations provided by the International Committee on Non-Ionizing Radiation Protection (ICNIRP) and the Institute of Electrical and Electronics Engineers (IEEE), (3) smart meter radio frequency studies conducted by other states such as California, Texas, Maine, and Vermont, (4) peer-reviewed scientific publications, and (5) smart meter and RF exposure related documents submitted to the Arizona Corporation Commission's eDocket. Based on the available information, ADHS found that:

- The majority of the countries determined their standards based on the recommendation of the ICNIP and IEEE. The values of specific absorption rate (SAR) and power density were established to prevent thermal effects from radio frequency radiation. No value was recommended for non-thermal effects because the ICNIP and IEEE, based on the available information, feel that the evidence from epidemiological and laboratory studies are not sufficient to identify there is a health hazard nor to be used as a basis to develop exposure guidelines.
- Russia set a much lower standard which was determined to prevent any possible biological consequences among the exposed population. The study was conducted by Russian scientists and the paper was written in Russian. ADHS was not able to review the report. The source indicated that the value was determined based on chronic immunology studies from a number of animal studies.

away from the RF emitter to be located in what is commonly referred to as the "far-field" zone of the radiation source, e.g., more than several wavelengths distance from a typical RF source. In the far field, the electric and magnetic fields are related to each other in a known way, and it is only necessary to measure one of these quantities in order to determine the other quantity or the power density. In closer proximity to an antenna, i.e., in the "near-field" zone, the physical relationships between the electric and magnetic components of the field are usually complex. In this case, it is necessary to determine both the electric and magnetic field strengths to fully characterize the RF environment. (Note: In some cases equipment used for making field measurements displays results in terms of "far-field equivalent" power density, even though the measurement is being taken in the near field.) At frequencies above about 300 MHz it is usually sufficient to measure only the electric field to characterize the RF environment if the measurement is not made too close to the RF emitter.

Power density is defined as power per unit area. For example, power density can be expressed in terms of milliwatts per square centimeter (mW/cm^2) or microwatts per square centimeter ($\mu W/cm^2$). One mW equals 0.001 watt of power, and one μW equals 0.000001

watt. With respect to frequencies in the microwave range and higher, power density is usually used to express intensity since exposures that might occur would likely be in the far-field. More details about the physics of RF fields and their analysis and measurement can befound in References 2, 3, 8, 21, 33, 34 and 35.

WHAT BIOLOGICAL EFFECTS CAN BE CAUSED BY RF ENERGY?

A biological effect occurs when a change can be measured in a biological system after the introduction of some type of stimuli. However, the observation of a biological effect, in and of itself, does not necessarily suggest the existence of a biological hazard. A biological effect only becomes a safety hazard when it "causes detectable impairment of the health of the individual or of his or her offspring" (Reference 25). There are many published reports in the scientific literature concerning possible biological effects resulting from animal or human exposure to RF energy.

The following discussion only provides highlights of current knowledge, and it is not meant to be a complete review of the scientific literature in this complex field. A number of references are listed at the end of this document that provide further information and details concerning this topic and some recent research reports that have been published (References 1, 3, 6, 7, 9, 14,15-19, 21, 25, 26, 28-31, 34, 36, 39-41, 47, 49 and 53).

Biological effects that result from heating of tissue by RF energy are often referred to as "thermal" effects. It has been known for many years that exposure to high levels of RF radiation can be harmful due to the ability of RF energy to heat biological tissue rapidly. This is the principle by which microwave ovens cook food, and exposure to very high RF power densities, i.e., on the order of 100 mW/cm^2 or more, can clearly result in heating of 6 biological tissue and an increase in body temperature.

Tissue damage in humans could occur during exposure to high RF levels because of the body's inability to cope with or dissipate the excessive heat that could be generated. Under certain conditions, exposure to RF energy at power density levels of 1-10 mW/cm^2 and above can result in measurable heating of biological tissue (but not necessarily tissue damage). The extent of this heating would depend on several factors including radiation frequency; size, shape, and orientation of the exposed object; duration of exposure; environmental conditions; and efficiency of heat dissipation.

Two areas of the body, the eyes and the testes, are known to be particularly vulnerable to heating by RF energy because of the relative lack of available blood flow to dissipate the excessive heat load (blood circulation is one of the body's major mechanisms for coping with excessive heat). Laboratory experiments have shown that short-term exposure (e.g., 30 minutes to one hour) to very high levels of RF radiation (100-200 mW/cm^2) can cause cataracts in rabbits. Temporary sterility, caused by such effects as

changes in sperm count and in sperm motility, is possible after exposure of the testes to high-level RF radiation (or to other forms of energy that produce comparable increases in temperature).

Studies have shown that environmental levels of RF energy routinely encountered by the general public are far below levels necessary to produce significant heating and increased body temperature (References 32, 37, 45, 46, 48 and 54). However, there may be situations, particularly workplace environments near high-powered RF sources, where recommended limits for safe exposure of human beings to RF energy could be exceeded.

In such cases, restrictive measures or actions may be necessary to ensure the safe use of RF energy. In addition to intensity, the frequency of an RF electromagnetic wave can be important in determining how much energy is absorbed and, therefore, the potential for harm. The quantity used to characterize this absorption is called the "specific absorption rate" or "SAR," and it is usually expressed in units of watts per kilogram (W/kg) or milliwatts per gram (mW/g). In the far-field of a source of RF energy (e.g., several wavelengths distance from the source) whole-body absorption of RF energy by a standing human adult has been shown to occur at a maximum rate when the frequency of the RF radiation is between about 80 and 100 MHz, depending on the size, shape and height of the individual. In other words, the SAR is at a maximum under these conditions. Because of this "resonance" phenomenon, RF safety standards have taken account of the frequency dependence of whole-body human absorption, and the most restrictive limits on exposure are found in this frequency range (the very high frequency or "VHF" frequency range). Although not commonly observed, a microwave "hearing" effect has been shown to occur under certain very specific conditions of frequency, signal modulation, and intensity where animals and humans may perceive an RF signal as a buzzing or clicking sound.

Although a number of theories have been advanced to explain this effect, the most widely-accepted hypothesis is that the microwave signal produces thermoelastic pressure within the head that is perceived as sound by the auditory apparatus within the ear.

- States conducting radio frequency studies have similar findings, based on scientific literature review or field measurements. Their results agreed that the thermal effects of radio frequency are well understood, and the current FCC standard is sufficient to provide an adequate protection to prevent thermal effects. In addition, no sufficient evidence to support a need for additional standards to protect the public from electronic meters.
- ADHS concurs with the findings from the other states. ADHS reviewed articles on the potential health risks from RF radiation, mainly from wireless communication The review examined the potential biological and health effects from exposure to RF fields from studies that have been published. The authors reviewed relevant research investigations in different areas: epidemiology studies, empirical studies in cell cultures and animals, and clinical human studies. An overall assessment was then conducted based on the aggregated evidence across reviewed areas. ADHS found that most experts agree that exposure to RF at high enough strengths for long enough time can result in adverse health outcomes from thermal effects. However, when discussing non-thermal adverse health outcomes, the literature is not clear.
- ADHS also reviewed articles published in the last five years that discussed the health concerns most noted by Arizona citizens. These health effects are: headaches, insomnia, cancer, ear pain/tinnitus, and fatigue. Most of the studies concluded that there was no association between RF exposure at low levels and adverse health outcomes. A couple of articles found weak associations Some studies called for additional research.

The entire conclusions made by the ADHS and their observations are null and void based on flawed data, incomplete research and outdated information.

When an ordinary citizen can do a better job of assuring the data presented is more up to date than a state agency whose sole purpose is to assure public safety then there is something drastically wrong with the system and those who are responsible to assure public health and safety.

Field Investigation:

ARRA conducted a field investigation to identify the levels of RF radiation emitted from different types of meters (i.e. analog, PLC, AMI, and AMR meters) The measurements were taken from single family homes, and apartment complexes at rural and urban areas. After receiving data from ARRA, ADHS conducted an assessment to evaluate the potential health risks associated with exposure to radio frequency radiation emitted from electronic meters (i.e. AMI and AMR meters.) Based on the available information, ADHS reached the following conclusions:

At best this was a field check, as it falls way short of being considered and investigation. If this is what the ARRA considers an investigation, then the credibility of the Agency should be in question as to their ability to safeguard the people of this state.

- The measured RF radiation emissions (in power density) from electronic meters are below the FCC standard of 6 watts per square meter (W/m^2).
- In general, the measured RF radiation emissions are higher from AMI and AMR meters. The measured RF radiation emission from analog and PLC meters are similar to the background levels.
- In general, for electronic meters, the measured RF radiation emissions are higher for apartment complexes when they are compared to single family homes.
- In general, for electronic meters, the measured RF radiation emission is higher from urban area when they are compared to those from rural area
- *Exposure to electric meters (AMI and AMR) is not likely to harm the health of the public.* This conclusion was reached because (1) none of the detected power densities exceeded the FCC standard of 6 W/m^2. This standard was determined based on thermal effects, and was set to prevent whole-body heat stress and excessive localized tissue heating; (2) available government assessments and scientific literature indicated that there is no consistent or convincing evidences to support a cause-and-effect relationship related to the exposures to the RF frequency (900 – 930 MHz) used by the smart meters ; (3) none of the detected power density exceeded the lowest available guideline of 0.1 W/m^2 (determined by Russia.) This value was determined to ensure that no exposure would cause any possible biological consequences among the exposed population.

As previously stated (repeatedly) the information used is neither accurate nor up to date by the IEEE standards they themselves use. Therefore any reference to those standards is not valid even by the IEEE standards.

Since the ARRA clearly states the following: under **R12-1-1403 A2** – "whether the registrant provided information requested by the agency to **determine if there are alternative methods of achieving the same or greater level of radiation protection**."

Since this is paramount to what this agency is supposed to advocate, then with the changes in technology, the Commission should consider that if those of the public who want to opt out of smart meters for health reasons, and are willing to procure a whole house monitoring system at their own expense; they should be free of any additional fees or charges by the utilities.

Further, since these devices will monitor ALL electrical power used 24/7/365 and re capable of transmitting that data to the utility. This would be at no cost to the utility and open up the ability to use all existing rate plans offered by the utility; rather be limited to be financially punished by the utility and placed on their highest rate tiers which increase utility costs by as much as 240% over previous years.

In this scenario, everyone wins – the utility has what they seek on a smart grid insofar as:

1) Total electrical usage accountability namely Time of Use,
2) They do not have to send anyone out to read the meter,
3) The cost of purchasing and installing the monitor unit is borne by the customer
4) The state is not liable for any violations of state and federal laws
5) In line electrical filter to assure the utility a clean signal for monitoring purposes (something that the utility itself does not provide)

The consumer also gets what they want:

1) A safe analog mechanical meter
2) No chance of immediate area microwave intrusion into their home from a smart meter other than overlapping microwave radiation from surrounding meters.
3) The ability to partake in all offered rate plans from the utilities for cost savings
4) No more fighting with the Commission to rectify obvious violations of the law.

The information on the devices available and their capabilities are attached to this report.

Then why didn't the ADHS quote this in their findings and err on the side of caution?

How can the ADHS come to the conclusion that AMI / AMR meters are "not likely to harm the health of the public," when their data choices are flawed and out of date? Why did they use the Russian limits then switch to the IEEE / FCC limits for their conclusions?

Why is it they chose to use only those studies, which back up their conclusions, and not of the rest of the conclusions drawn by the world's scientific community? Is the Commission willing to take the chance and put the state in jeopardy based on conclusions that state the these meters are "not likely" to harm the public? If the ADHS is so sure of their findings then why don't they state unequivocally that smart meters ARE safe and pose NO danger to the public? Why is it that they protect themselves with half baked easy out statements that leave them a legal out in case they are proven wrong. Either they stand by their findings in perpetuity or they don't.

Neither the Commission, ADHS or ARRA can afford to be wrong here and have you put the public at risk.

1. Article: "Electromagnetic and Radiofrequency Fields Effect on Human Health." The American Academy of Environmental Medicine (AAEM). 2008.

   Main Points Stated by the Article:

   - In the last 20 years, physicians began seeing patients who reported that electric power lines, televisions, and other electrical devices caused a wide variety of symptoms.
   - Multiple studies correlate RF exposure with diseases such as cancer, neurological disease, reproductive disorders, immune dysfunction, and electromagnetic hypersensitivity.
   - Exposure limits determined by the FCC and other regulatory agencies do not account for effects from non-thermal radiation.

   ADHS's Response: AAEM are not recognized by the American Board of Medical Specialties.

The sheer arrogance and audacity of the ADHS remark in stating "that the American Academy of Environmental Medicine is NOT recognized by the American Board of Medical Sciences" is like saying that they are experts in a field where they have little or no knowledge.

What medical background do any of the personnel on staff at the ADHS have to discount work and studies performed by certified board members of the medical community who focus on Environmental medicine?

2. Article: Loren Vanderlin. "Update and Review of Research on Radiofrequencies: Implications for a Prudent Avoidance Policy in Toronto." Toronto Public Health. November 2007.

Main Points Stated by the Article:

- Despite limitations in the body of research to date, the possibility of harmful health effects from RF exposures cannot be ruled out.
- Studies of the impacts on children from cell phone RFs, while limited in number, do not rule out the possibility that children require greater protection from RF exposure.
- Research in populations near cell phone base stations in Europe indicates that some people living within about 300 meters of a base station are more likely to experience symptoms, such as headache, memory changes, dizziness, tremors, depression, and sleep disturbance.
- In the face of uncertain risks, prudent avoidance is still the best approach to minimize public exposure from the new and increasing number of RF sources.
- In response to this article, Toronto Public Health (TPH) reviewed the predicted RF values **provided by companies applying to install new cell phone base stations in Toronto and requested that providers keep RF emission levels 100 times below Safety Code 6, Health Canada's public exposure guideline. From its review of recent health evidence, TPH notes that the majority scientific opinion indicates that the health risk to the public from** cell towers and other telecommunications sources of RFs is low.

ADHS Response: Although this article infers the biological feasibility of RF exposure and non-thermal effects, this article does not directly relate to the goals of this review. ADHS focused on RF exposures in the home. RF exposure at or near cell towers tend to be at much higher power densities than that which are measured near electronic meters, and is therefore not within the scope of this report.

This is nothing short of an absolute lie! Earlier on the ADHS clearly admitted that they did NOT draw data from inside any home, now they state they focused on microwave exposure within the home. So which is the lie? What is the truth?

Since it is obvious that the ADHs does not realize that each smart meter broadcasts its signal in a 360 radius and NOT line of sight or directional – they are ill equipped to make this statement. Each smart meter has a broadcast range of 21 miles; and each meter overlaps the other from home to home or complex to complex, so each of the points made here are not only relevant, but accurate and must be considered.

The end result of this study, is simple:

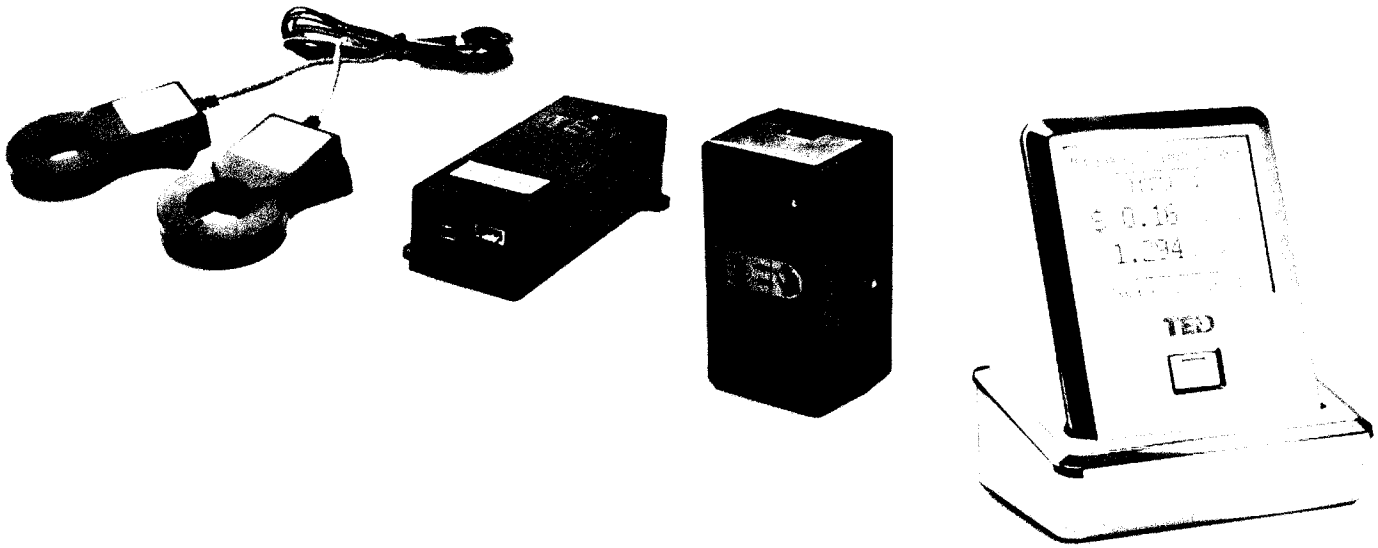
A) It is flawed
B) It is incompetent
C) It is incomplete
D) It is not performed In Accordance With Time Weighted Average studies professionally conducted

E) It does not come to a definitive answer that either the Commission or the ADHS will stand on

F) It is open ended and thus a farce or fraud on the people of the state and the Commission.

With respect,

Doug Staab
15805 North 45th Place
Phoenix, AZ 85032



Worldwide Published Studies Demonstrate Health Impacts of

Wireless (RF/Microwave) Radiation

Below are summaries of Research Abstracts on RF/MW radiation taken from National Library of Medicine Website (PUBMED : www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed
The Summaries below are divided by categories of most prominent effects on the human body. The studies are further categorized by type of study: In-Vitro – cellular lab study; In-Vivo – alive subjects in lab studies; Epidemiological – population sampling of real life conditions. Included with each summaries is the citation of the study: title(in *italics*); authors; research institution; date of study; country of origin; publication

The 3 Bar heading highlights the following information in the study:

Physical area affected &/or sypmptoms experienced	EMF Device Used	Subject of study

Brain function changes

Brain Wave Changes	Mobile Phones	humans

In-Vivo

1) The study finds that 7 frequencies in the human brain wave band from 1-32 Hz are affected by radiation equal to the signal intensity and frequency of mobile phones in talk mode. *"Human brain wave activity during exposure to radiofrequency field emissions from mobile phones".* D'Costa H, Trueman G, Tang L, Abdel-rahman U, Abdel-rahman W, Ong K, Cosic I.: School of Electrical & Computer Engineering, RMIT University, Melbourne, **Australia;** Australia Phys. Eng Sci Med. **2003** Dec; 26(4)162 –7 [2]

Brain Wave Changes	Mobile Phones	hypothesis

2) The authors **hypothesize** that the brain absorbs the RF wave length from digital cell phone transmission at the 1800 Mhz frequency band. "Brain cells and tissues demodulate the cell-phone's audio frequencies from the radio frequency carrier. Low audio in the ranges of alpha and beta waves are affected by these radio waves and thereby influence brain function. This hypothesis states the case for a **precautionary policy."**
"Cellular telephones and effects on the brain: The head as an antenna and brain tissue as a radio receiver." Weinberger Z, Richter ED.; Jerusalem College of Technology, Jerusalem, **Israel;** Jrnl - Med Hypotheses **2002** Nov;59(6):703-5 [22]

In Vitro

Brain damage	cell phones	mice

3) THe study exposed rats brain neural cells (nervous system) to a GSM cell phone (PCS equivalent) frequency (900 or1800 Mhz) of different power strengths for 2 hrs. It found highly significant evidence for neuronal damage in the cortex, hippocampus, and basal ganglia in the brains of exposed rats. The study did not identify if all power strengths caused the damage.
"Nerve cell damage in mammalian brain after exposure to microwaves from GSM mobile phones;"; Salford LG, Brun AE, Eberhardt JL, Malmgren L, Persson BR.; Department of Neurosurgery, Lund University, The Rausing Laboratory and Lund University Hospital, Lund, **Sweden**; Jrnl- Environ Health Perspect. **2003** Jun;111(7):881-3; discussion A408. [36]

In_Vivo

Brain slow wave affected	Cell phones	humans

3a) Using an improved method for measuring EEG, the study shows how the slow wave activity of the brain is raised after short period of cell phone use. "Spatial distribution of EMF was especially concentrated around the ipsilateral eye adjacent to the basal surface of the brain." The effects are more pronounced in children. However the study showed after approximately 15– 20 minutes of non-use the effect had disappeared. This study demonstrates the need for more long term experimental studies. *"Effects of high-frequency electromagnetic fields on human EEG: a brain mapping study."* ; Kramarenko AV, Tan U.; Central Clinic Hospital N5, Kharkov, **Ukraine;** Jrnl - Int J Neurosci. **2003** Jul;113(7):1007-19. [48]

Heart and Circulatory Changes

In Vivo

Brain Blood flow changes	in lab[1] ELFs (extreme low frequency) – closer to power line EMFs	depressed humans

4) This study found effects on the cerebral blood flow of depressed patients from EMF (electromagnetic fields) stimulation in the ELFs (Extremely low frequencies) bands of the frequency spectrum, specifically 1 and 15 Hz. Radio & Microwave frequencies carry an ELF component as part of their communication by-product. In many studies this component of the radio wave has been found to be most troublesome to the body. The study did not state the power level of the signal(frequency), so it may be difficult to correlate to real world exposures.
"High (15 Hz) and low (1 Hz) frequency transcranial magnetic stimulation have different acute effects on regional cerebral blood flow in depressed patients." Psychol Med . **2003 Aug;33** (6); 997-1006; Loo CK, Sachdev PS, Haindl W, Wen W, Mitchell PB, Croker VM, Malhi GS. :School of Psychiatry, University of New South Wales, **Australia** [3]

Epidemiological

Blood Pressure & Nervous system	Radio equipment	technicians & broadcast workers

5) The study covered workers employed in transformer and distribution stations, medium wave transmitting stations, radio-service and radio and TV multichannel broadcasting stations. Changes in the circulatory system were observed with a significant relationship between exposure parameters and blood pressure and nervous system disorders. The longer the workers worked at those jobs the greater the occurrence of changes in these disorders.
[Article in Polish] *"Biological effects and health risks of electromagnetic fields at levels classified by INCRIP as admissible among occupationally exposed workers".* Bortkiewicz A, Gadzicka E, Zmyslony M.; Nofer Institute of Occupational Medicine, Lodz, **Poland, 2003** [34]

Epidemiological

Heart rate & Blood Pressure Affected	Radio equipment	technicians & broadcast workers

6) The study examined heart rate variability and blood pressure of radio technicians and operators. It found certain groups of radio workers showed significant greater abnormalities in these parameters compared to unexposed populations.
"Evaluation of selected functional circulation parameters of workers from various occupational groups exposed to electromagnetic fields of high frequency. III. 24-h monitoring of arterial blood pressure."; Gadzicka E, Bortkiewicz A, Zmyslony M, Palczynski C.; Zakladu Fizjologii Pracy i Ergonomii, Instytutu Medycyny Pracy, Lodzi, **Poland**; Jrnl - Med Pr. **1997**;48(1):15-24.[32]

In-Vivo

Brain Blood flow affected	digital cell phones & cell towers	humans

7) The study examined regional cerebral blood flow (rCBF) from exposures to 2 different signals: digital cell phone and base station signals for 12 healthy young men. A sham exposure was included. The study found that only cell phone signals induced changes in rCBF because of their pulse modulated wave. They state " that pulse modulation of RF EMF signals is necessary to induce changes in the waking and sleep EEG, and substantiates the notion that pulse modulation is crucial for RF EMF-induced alterations in brain physiology."

*"Exposure to pulse-modulated radio frequency electromagnetic fields affects regional cerebral blood flow." ; **Huber R, Treyer V, Schuderer J, Berthold T, Buck A, Kuster N, Landolt HP, Achermann P.**; Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland.: Jrnl - Eur J Neurosci. 2005 Feb;21(4):1000-6.*[42]

DNA, Chromosomal and Cellular Changes

In-Vivo

DNA Damage	in lab cell phone frequencies	mice

8) This study showed that exposure in mice to cell phone frequencies and signal strength can have a detrimental effect on DNA repair mechanisms after a long duration of exposure. The authors comment that the sample size was small and should be repeated. *"Effect of exposure to 900 MHz radiofrequency radiation on intrachromosomal recombination in pKZ1 mice."* Sykes PJ, McCallum BD, Bangay MJ, Hooker AM, Morley AA.; Department of Haematology and Genetic Pathology, Flinders University and Medical Centre, Bedford Park, South **2003, Australia** 5042..[4]

In-Vitro

Cellular stress protein affects	In lab RF/Microwave transmitter	cell culture

9) The study examines the effects of RF/ MW frequency radiation on cell proliferation under higher room temperatures, 35 & 39 degrees centigrade. Those cells exposed to RF/MW radiation showed significant changes, while controls exposed under same room temperature differences showed no change. This study was rejecting the claim that external temperatures effect cell changes and supports the evidence that RF/MW frequencies without higher room temperatures induce cell changes. This study also supports the studies that show heat shock proteins (stress related proteins) in the body are affected when exposed to RF/MW signals.
"The effects of radiofrequency fields on cell proliferation are non-thermal"; S.. Velizarova, P. Raskmarkb and S. Kwee~'; jrnl - Bioelectrochemistry and Bioenergetics Volume 48,, Issue 1, February **1999**, Pages 177-180; Bulgaria, Denmark [13]

In-Vitro

Cellular Gene affects	in lab RF/MW transmitter	newborn rats

10) The study examines exposure of rats to 9.4Ghz frequency at a low 5microwatt/cm^2 power levels on gene markers in kidney development of newborn rats. This power level can be found in and around hot spots of broadcast stations, lower than that emitted by cell phones. Although 9.4Ghz is a higher frequency signal than a cell phone, the study suggests cell phone frequencies interfere with certain types of gene expression during early gestation and results in aberrations in the kidney development of the newborn rats.

"Bone morphogenetic protein expression in newborn rat kidneys after prenatal exposure to radiofrequency radiation."; Pyrpasopoulou A, Kotoula V, Cheva A, Hytiroglou P, Nikolakaki E, Magras IN, Xenos TD, Tsiboukis TD, Karkavelas G.; Laboratory of Pathology, Department of Medicine, School of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, **Greece;** Jrnl - Bioelectromagnetics. **2004** Apr;25(3):216-27. [20]

In- Vitro

cellular brain protein affects in lab AM signals rats

11) The study examines certain enzymes in the developing rat brain after exposure to AM frequency band (500 to 1600 KHZ) at power levels found close to AM radio broadcast antennas. A significant decrease in the enzyme level was observed in the exposed group. "These results indicate that this type of radiation could affect membrane bound enzymes associated with cell signaling, proliferation and differentiation. This may also suggest an affect on the behavior of chronically exposed rats."

"Radio frequency radiation effects on protein kinase C activity in rats' brain."; Paulraj R, Behari J. ; School of Environmental Sciences, Jawaharlal Nehru University, New Delhi 110067, **India.;** Jrnl - : Mutat Res. **2004** Jan 12;545(1-2):127-30. [21]

In Vitro

cellular CNS (central nervous system enzyme) affects cell phone cell cultures

12)"This paper demonstrates... that radio frequency (RF) radiations irreversibly affect the structural and biochemical characteristics of an important CNS (Central Nervous System) enzyme" in laboratory cell cultures. "These results were obtained by using a commercial cellular phone to reproduce the reality of the human" exposure.

"Structural and kinetic effects of mobile phone microwaves on acetylcholinesterase activity." Barteri M, Pala A, Rotella S.: Dipartimento di Chimica- Universita degli Studi di Roma "La Sapienza" Piazzale Aldo Moro 5, 00185 Roma, **Italy;** Jrnl - Biophys Chem. **2005** Mar 1;113(3):245-53 [25]

Epidemiology

White blood cells higher radar human population2

13) The study showed higher white blood cell counts of WWII radar workers exposed to RF/MW radiation at higher levels and longer durations than the average population. The blood counts showed increasingly elevated as the duration of exposure increased.

"Time-dependent hematological changes in workers exposed to electromagnetic fields.";Marino AA.: Department of Orthopaedic Surgery, Louisiana State University Medical Center, Shreveport, La. **USA** 71130-3932.; Jrnl - Am Ind Hyg Assoc J. **1995** Feb;56(2):189-92.U [61]

In Vitro

cellular stress proteins affects in lab high microwave levels human cell cultures

14) The study found that certain heat shock proteins (protein level of phosphorylated Hsp27 (78Ser)) were significantly decreased at SAR 10W/kg at 1950 MHZ similar to cell phone frequencies but much higher power levels. However, at lower power levels 1 and 2W/kg similar to cell phone power levels, there was no effect on these proteins. Exposure times were 1 to 2 hrs. Heat shock proteins are related to the stress mechanisms of the body.

"Effects of exposure to a 1950 MHz radio frequency field on expression of Hsp70 and Hsp27 in human glioma cells.": Miyakoshi J, Takemasa K, Takashima Y, Ding GR, Hirose H, Koyama S.; Department of Radiological Technology, School of Health Sciences, Faculty of Medicine, Hirosaki University, Hirosaki, **Japan**; Jrnl - Bioelectromagnetics. **2005** May;26(4):251-7.[27]

In-Vitro

DNA damage in lab higher microwave human blood cells

levels

15) The study evaluated the toxicity of human blood cells from exposure to different power levels in the frequency levels of 837 MHz and 1908 Mhz, analog & digital cellular phones frequencies. Compared to controls it found 4-fold damage to blood cells after 24 hour exposure by both those frequencies at the high power levels (SARs 5 to 10 w/kg), but not at lower power level (SAR 1 w/kg). Most modern cell phones induce SARs between 1 & 2 w/kg. It found no significant differences at any power level between controls and exposed blood cells for shorter exposure durations than 24 hours.
"Genotoxicity of radiofrequency signals. I. Investigation of DNA damage and micronuclei induction in cultured human blood cells." Tice RR, Hook GG, Donner M, McRee DI, Guy AW.; ILS, Inc., Research Triangle Park, North Carolina 27709, **USA** ; Jrnl - Bioelectromagnetics **2002** Feb;23(2):113-26 [67]

In-Vitro

cellular enzyme affects in lab RF frequency yeast cells

16) The study demonstrates the protective effect of electromagnetic radiation (40.68 MHz at 15 and 30 Watt) on the survivability of yeast cells. The cells showed greater activity of certain types of intracellular enzymes, as well as greater stability of electrostatic characteristics of the cell surface.
"Protective action of electromagnetic radiation (40.68 MHz) on Saccharomyces cerevisiae UCM Y-517"; Podgorskii VS, Voichuk SI, Gromozova EN, Gordienko AS.; Jrnl - Mikrobiol Z. **2004** Sep-Oct;66(5):48-56. **Russia** [35]

In-Vivo

electrosensitivity affects in lab RF frequency predisposed rats

17) Using a specially bred strain of rats the study concludes that electrosensitivity from radio waves is possible and genetically predisposed. *"Genetic susceptibility to radiation."*; Hall EJ, Brenner DJ, Worgul B, Smilenov L.; Columbia University Medical Center, College of Physicians and Surgeons, Center for Radiological Research, New York, NY 10032-3795, **USA;** Jrnl - Adv Space Res. **2005**;35(2):249-53.[54]

In-Vitro

cellular stress proteins affects in lab RF transmitter chick embryos

18) THe study finds that chick embryos exposed to ELF (extremely low frequency 1- 120Hz) and RF (radio frequency) EMFs at cell phone power levels induce a decrease in HSP70 (heat shock proteins) levels. The resulting decline decreases protection against stress and suggests " a mechanism which could enhance the probability of cancer and other diseases" *"Chronic electromagnetic field exposure decreases HSP70 levels and lowers cytoprotection."*; Di Carlo A, White N, Guo F, Garrett P, Litovitz T., Feb **2002;** Vitreous State Laboratory, Catholic University of America, Washington, DC 20064, **USA.** [58]

In Vivo

2 cell phone frequencies MHz

DNA affects & GHz human blood cells

19) Researchers compared the responses of healthy and hypersensitive people to the old and new cell phone signals. Both groups reacted to the new Ghz UMTS Broadband microwaves, not to the old Mhz GSM signal. The Ghz frequency had an effect on chromatin and inhibited formation of DNA double-strand breaks co-localizing DNA repair foci. However hypersensitive people showed a different response in DNA repair foci from both signals compared to healthy controls.
Microwaves from UMTS/GSM mobile phones induce long-lasting inhibition of 53BP1/gamma-H2AX DNA repair foci in human lymphocytes; Belyaev IY, Markovà E, Hillert L, Malmgren LO, Persson BR.; Department of Genetics, Microbiology and Toxicology, Stockholm University, Stockholm, **Sweden**..; Bioelectromagnetics. **2009** Feb;30(2):129-41. [102]

In Vivo

Blood cells – stress respons, genotoxic effects	Cell phones	Hypersensitive & normal humans

19a) The study found Microwaves from cell phones affect chromatin conformation and 53BP1/gamma-H2AX foci of human lymphocytes (blood cells) of both proclaimed hypersensitive people as well as healthy subjects. These biological markers are indicative of stress response and genotoxic effects. Healthy people did not show a distinctly different response than hypersensitive people.
Microwaves from GSM mobile telephones affect 53BP1 and gamma-H2AX foci in human lymphocytes from hypersensitive and healthy persons; Markovà E, Hillert L, Malmgren L, Persson BR, Belyaev IY; Department of Genetics, Microbiology and Toxicology, Stockholm University, Stockholm, **Sweden**; Environ Health Perspect, **2005** Sep 113(9):1172-7 **[103]**

Organ, Endrocrine and Enzyme changes

In-Vitro

Sperm DNA damage in lab cell phone frequencies male mice

20) The semen of male mice was exposed to cell phone frequencies and power levels over a period of days. The study "revealed statistically significant damage to both the mitochondrial genome and the nuclear beta-globin locus" in the DNA semen of mice *"Impact of radio frequency electromagnetic radiation on DNA integrity in the male germline"*. Int J Androl. **2005 Jun** 28(3):171-9 Aitken RJ, Bennetts LE, Sawyer D, Wiklendt AM, King BV. : ARC Centre of Excellence in Biotechnology and Development, Discipline of Biological Sciences, and Hunter Medical Research Institute, Newcastle, NSW, **Australia.** [6]

Epidemiological

Sperm quality affects occupational RF exposure human males

21) THe study examined the semen quality of male occupationally RF exposed workers. It measured 33 parameters of semen quality and four serum hormones of 12 male exposed and 34 non- exposed. It observed minor differences and suggests further studies may be warranted.
Grajewski B; Cox C; Schrader SM; Murray WE; Edwards RM; Turner TW; Smith JM; Shekar SS; Evenson DP; Simon SD; Conover DL ; National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, OH 45226, **USA.**; Jrnl - J Occup Environ Med **2000 Oct**;42(10):993-1005 [66]

In Vivo

Kidney damage antioxidant reversal in lab cell phone frequencies rats

22) The study finds that propolis (Caffeic acid phenethyl ester), a flavonoid, anti-oxidant, free radical scavenger derived from honeybees, reduces renal (kidney) impairment in rats from cell phone type radiation by 27%.. It does this partially by blocking oxidative processes in the kidneys.
"A novel antioxidant agent caffeic acid phenethyl ester prevents long-term mobile phone exposure-induced renal impairment in rat."; Ozguner F, Oktem F, Ayata A, Koyu A, Yilmaz HR.; Department of Physiology, School of Medicine, Suleyman Demirel University, P. K. 13, Isparta, 32100, **Turkey**; Jrnl - Mol Cell Biochem. **2005 Sep**;277(1-2):73-80 [45]

.

In-Vivo

Thyroid affects in lab cell phone frequencies rats

23) The study finds that electromagnetic radiation similar to that emitted by 900 MHz cellular phones has significant effects on certain thyroid hormones in a specific breed of rats. New digital phones broadcast at around 1900 – 2400 MHz.

"Effects of 900 MHz electromagnetic field on TSH and thyroid hormones in rats."; Koyu A, Cesur G, Ozguner F, Akdogan M, Mollaoglu H, Ozen S.; Department of Physiology, Suleyman Demirel University, School of Medicine, 32260 Isparta, **Turkey**; Jrnl - : Toxicol Lett. **2005 Jul** 4;157(3):257-62. Epub 2005 Apr 11; [47]

In-Vivo

Melatonin levels in lab magnetic fields 2 MS male/female patients

24) The study examines opposite effects on the yawning reflex of two MS patients after administration of yawning drug, ketanserin, and the application of picotesla EMFs. Under the drug the female MS patient stopped yawning after EMF application, while male MS patient yawning increased after EMF application. The study believes EMFs had an effect on melatonin levels, known to effect sleepiness, increasing levels for the male and decreasing them for female. *Bidirectional effect of electromagnetic fields on ketanserin-induced yawning in patients with multiple sclerosis: the role of melatonin*: Sandyk R.; NeuroCommunication Research Laboratories, Danbury, CT 06811, **USA**.; Intl J Neuroscience **1996** Mar;85(1-2):93-9. [93]

In-Vitro

Sperm motility changes cell phones humans

25) The study examines the effects of sperm degeneration from 27 male volunteers when their sperm was exposed in vitro to EMR from cell phones. THe study found no difference in sperm concentration, but, in contrast to controls, the study found a subtle but statistically significant reduction in sperm motility (movement) in 2 categories, rapid progressive and slow progressive sperm movement. It also showed an increase in the no-motility category of sperm movement in contrast to controls..
Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study; Erogul O, Oztas E, Yildirim I, Kir T, Aydur E, Komesli G, Irkilata HC, Irmak MK, Peker AF.; Biomedical and Clinical Engineering Centre, Gulhane Military Medical Academy, Etlik, Ankara, **Turkey**; Arch Med Res. **2006 Oct**;37(7):840-3. **[94]**

Neurological & Well Being Effects(sleep, stress, headaches, tinnitus, etc.)

Epidemiological

Stress hormones & circadian rhythm (sleep/wake cycle) affected Telecommunication equipment worker population

26) The study examines certain stress hormones of satellite telecommunications operators. "The long term effect of the exposure to low-level RF EM radiation evoked pronounced stress reaction with changes in the circadian rhythm ... and increased variability of catecholamines secretion". Circadian rhythms are part of our sleep cycles.
"*The effect of low level radiofrequency electromagnetic radiation on the excretion rates of stress hormones in operators during 24-hour shifts.*" Cent Eur J Public Health **2002** Jun; 10(1-2): 24-8 ; Vangelova K, Israel M, Mihaylov S.; Laboratory of Physiology, Psychology and Ergonomics, National Center of Hygiene, Medical Ecology and Nutrition, 15 Dimiter Nestorov Boul., 1431 Sofia, **Bulgaria** [8]

Epidemiological

Headaches, Insomnia, amnesia increases Radio equipment worker population

27) The study uses VHF (Very high frequencies - 170 Mhz) , a frequency found in the low FM radio band, to evaluate the health effects of radio operators. It finds "the incidences of symptoms such as headache, insomnia and amnesia etc. was significantly higher in experimental group. Low power levels of VHF radiation can decrease the nervous system function in occupationally exposed personnel and induce increases in some kinds of enzymes and immunoglobulins." *"Effect of low intensity and very high frequency electromagnetic radiation on occupationally exposed personnel"* Zhonghua Lao Dong Wei Sheng

Zhi Ye Bing Za Zhi: Yuan ZQ, Li F, Wang DG, Wang Y, Zhang P. **2004 Aug** 22(4); 267-9 : Epidemic Prevention Brigade, General Logistics Department, PLA, Beijing 100039, **China** [12]

Epidemiological

Sleep, headaches, depression, dizziness, loss of memory increases	less 300 feet from cell transmitter	human population

28) This is a population study surveying 530 people living in the vicinity of cellular base stations (cell towers), on 18 Non Specific Health Symptoms. Comparisons of health symptom complaints, in relation to gender and the distance from cell site, revealed significant increases as compared to people living > 300 meters or not exposed to cell site: those living less than 300 mtrs for tiredness, less than 200 m for headache, sleep disruption, discomfort, etc., less than 100 m for irritability, depression, loss of memory, dizziness, libido decrease, etc. Women, significantly more often than men, complained of headache, nausea, loss of appetite, sleep disruption, depression, discomfort and visual disruptions.
[Article in French] "Study of the health of people living in the vicinity of mobile phone base stations. I. Influences of distance and gender; Santini R, Santini P, Danze JM, Le Ruz P, Seigne M.; Institut national des sciences appliquees, laboratoire de biochimie-pharmacologie, batiment Louis-Pasteur, 69621 cedex, Villeurbanne, **France**; Jrnl -Pathol Biol (Paris). **2003** Sep;51(7):412-5. [15]

In-Vivo

Sleep disturbances & heart rate variability increases	digital cell phone	humans

29) The study expounds on 2 prior studies which showed the effects of exposure from digital cell phones (900 Mhz) on sleep parameters and heart rate variability. The phones' power levels induced SARs of 1 w/kg in the body, a typical SAR found from exposure to most cell phones. The studies showed varying degrees of differences between the non- exposed, and the exposed in the sleep stages and heart rate variability of 9 healthy subjects.
"Radio frequency electromagnetic field exposure in humans: Estimation of SAR distribution in the brain, effects on sleep and heart rate"; Huber R, Schuderer J, Graf T, Jutz K, Borbely AA, Kuster N, Achermann P.; Institute of Pharmacology and Toxicology, University of Zurich, Zurich, **Switzerland**.; Jrnl - Bioelectromagnetics. **2003** May;24(4):262-76. [42]

Epidemiological

Hearing loss	vicinity radio transmitter	humans

30) The study demonstrates the hearing loss effect in those individuals who work at and live near radio/television transmitter stations, in contrast to control groups of similar work regimes, lifestyles and socioeconomic class.
"*Occupational safety: effects of workplace radiofrequencies on hearing function.*";Oktay MF, Dasdag S, Akdere M, Cureoglu S, Cebe M, Yazicioglu M, Topcu I, Meric F.; Department of Otolaryngology, School of Medicine, Dicle University, Diyarbakir, **Turkey**.; Jrnl - Arch Med Res. **2004 Nov-Dec**;35(6):517-21. [46]

In_Vivo

Stress reactions	in lab radio transmitter	rats

31) The study examines stress reaction in rats exposed to RF EMFs. It found exposed rats were less adaptive and had higher stress reactions to stressful situations.
"Changes in reactions in rats during hypokinesia and electromagnetic irradiation of ultrahigh frequency" [Article in Ukrainian]; Temur'iants NA, Chuian OM, Verko NP, Moskovchuk OB, Tumaniants OM, Shyshko OIu, Min'ko VA, Kurtseitova EE., ; Tavritcheskiy University by V.I. Vernadsky, Sympheropol, **Ukraine**; Jrnl - Fiziol Zh. **2003**;49(1):87-93. [49]

In_Vivo

Sleep brain waves & circadian
rhythms affect in lab radio transmitter humans

32) A Russian study showed how certain frequencies of EMFS rffect brain wave patterns which effect sleep patterns. The abstract does not identify the EMF frequencies or power levels used. It cites only that the frequencies were pulsed in the "ultra-broadband and ultrashort frequency range (somewhere in 900 Mhz & higher frequency band) with a repetition frequency of 6 Hz". The brain's theta rhythms and circadian rhythms were disturbed, which affect sleep quality.

Actions of pulsed ultra-broadband electromagnetic irradiation on the EEG and sleep in laboratory animals.; Petrova EV, Gulyaeva NV, Titarov SI, Rozhnov YV, Koval'zon VM.; Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, 117865 Moscow, **Russia;** Neurosci Behav Physiol. **2005** Feb;35(2):165-70; **[90]**

Epidemiological

sleep, memory, dizziness,
depression, tremors,
problem solving, attention
affected cell antennas humans

33) Researchers found 2 to 3 times higher incidence of neurobehavioral disorders in a population 85 people living below and opposite cellular antennas on apartment building roof, versus a control group of 80 people living 2 km away from the antenna site. Exposed group experienced higher incidence of sleep disturbances, memory changes, dizziness, depressive symptoms, tremors, Lower performance was found in problem solving, attention & short term auditory memory tests for the exposed group, especially those living across the antenna site. Power levels varied from 2 to 6 μw/cm2 across antenna, vs .1 μw/cm2 for those inhabitants living in the apartments below antenna. An emission reading .1 μw/cm2 is almost 10 times lower than cell phones and commonly found for those living near cell or broadcast towers.
"Neurobehavioral effects among inhabitants around mobile phone base stations" G. Abdel-Rassoul *, O. Abou El-Fateh, M. Abou Salem, A. Michael, F. Farahat, M. El-Batanouny, E. Salem; Community, Environmental and Occupational Medicine Department, Faculty of Medicine, Menoufiya University; Shebin El-Kom, **Egypt**; Received October **2005**; **[99]**

In Vivo

Brain dopamine affected in lab ELF/ EMF application rats

34) This study on rats shows how extremely low frequency magnetic field (ELF MF) reduce the reactivity of central dopamine D(1) receptors in rats by showing a reduction of irritability and oral activity. The rats had dopamine neurons chemically damaged by 6-hydroxydopamine (6-OHDA). This animal model showed similar dopamine damage exhibited in Parkinson's disease patients.
"Influence of alternating low frequency magnetic fields on reactivity of central dopamine receptors in neonatal 6-hydroxydopamine treated rats"; Sieron A, Brus R, Szkilnik R, Plech A, Kubanski N, Cieslar G.; Clinic of Internal Diseases and Physical Medicine, Silesian Medical University in Katowice, Zabrze, **Poland**; Bioelectromagnetics **2001** Oct;22(7):479-86. **[98]**

Epidemiological

Sleep complaints cell towers human population

35) A study of 3526 people analyzing the well being responses to cell tower exposures. Questions pertaining to sleep disturbances, headaches, health complaints and mental and physical health were analyzed. A dosimeter measuring different RF-EMF signal strengths was used. There was no difference in health scores between exposure assessments. People who self reported adverse health effects had greater sleep disturbances.
"Mobile phone base stations and adverse health effects: phase 2 of a cross-sectional study with measured radio frequency electromagnetic fields".; Berg-Beckhoff G, Blettner M, Kowall B, Breckenkamp J, Schlehofer

B, Schmiedel S, Bornkessel C, Reis U, Potthoff P, Schüz J; Department of Epidemiology and International Public Health, Faculty of Public Health, University of Bielefeld, **Germany**; Occup Environ Med. **2009** Feb;66(2):124-30. **[100]**

Epidemiological

Behavioral affects | cell phones | children population

36) Danish mothers of 13,159 children completed a questionnaire reporting their use of cell phones during pregnancy as well as current cell phone use by the child. Behavioral problems were observed for children who had possible prenatal or postnatal exposure to cell phone use. After adjustment for potential confounders, the odds ratio for a higher overall behavioral problems score was 1.80 in children with both prenatal and postnatal exposure to cell phones.
"Prenatal and postnatal exposure to cell phone use and behavioral problems in children"; Divan HA, Kheifets L, Obel C, Olsen J.; Department of Epidemiology, UCLA School of Public Health, University of California, Los Angeles, CA 90095-1772, **USA**.; Epidemiology. **2008** Jul;19(4):523-9.**[103]**

Cancer, Lymphomas and Tumor Formations

Epidemiological

Cancers higher: eye, testes, nasal, non - Hodgkin's lymphoma, and breast | Electronic equipment | worker population

37) Technicians with higher levels of RF exposures, between 10 to 100 microwatts/centimeter^2 ($\mu w/cm^2$) showed a high incidence of melanoma of the eye, testicular cancer, nasopharyngioma, non-Hodgkin's lymphoma, and breast cancer. These health effects were also found in the 20-37 age group, an age group that were not on the job as long as would have been expected for those cancers to develop, predicating that high powers levels can shorten the cancer latency period.
Jrnl - Int J Occup Environ Health **2000** Jul-Sep;6(3):187-93; Richter E; Berman T; Ben-Michael E; Laster R; Westin JB; Unit of Occupational and Environmental Medicine, Hebrew University-Hadassah Medical School, Jerusalem POB 12272, **Israel.** **[23]**

Epidemiological

Breast Cancer higher | Radio & Telegraph equipment | worker population

38) The study tabulated the incidence of breast cancer among radio and telegraph workers from 1961 to 2003. The frequency they were exposed to ranged from 405 Khz to 25 Mhz. The under 50 year olds had a lower incidence of breast cancer than those 50 years and older. However both showed a significantly higher incidence than the normal population.
"Follow-up of radio and telegraph operators with exposure to electromagnetic fields and risk of breast cancer."; Kliukiene J, Tynes T, Andersen A.; The Cancer Registry of Norway, Institute of Population-based Cancer Research, Montebello, NO-0310 Oslo, **Norway, 2003** **[29]**

Epidemiological

Non- Hodgkin's lymphoma higher | telecommunications & transport industry | worker population

39) The study tracked over 2.8 million workers in Sweden from 1971 to 1989 to observe the incidence of Non- Hodgkin's lymphomas. The highest risk was observed in telecommunications and transport workers. The authors explain the higher risk by their exposure to electromagnetic radiation.
"Non-Hodgkin's lymphomas and occupation in Sweden."; Cano MI, Pollan M.; Cancer Epidemiology Unit, National Centre for Epidemiology, Carlos III Institute of Health, Madrid, **Spain.**: Jrnl - Int Arch Occup Environ Health. **2001** Aug;74(6):443-9. **[38]**

Epidemiological

Melanoma higher | FM Transmitters | human population

40) This study examined the possible link between melanoma and proximity to FM broadcasting transmission sites in 4 different countries. A correlation was found between the higher incidence of melanoma and the number of nearby FM transmitters. *"Melanoma incidence and frequency modulation (FM) broadcasting."*; Hallberg O, Johansson O.; Department of Neuroscience, Karolinska Institute, Stockholm, **Sweden;** Jrnl - Arch Environ Health **2002** Jan-Feb;57(1):32-40 **[40]**

In-Vivo

Malignant Tumors higher | in lab cell phone frequencies & levels | rats

41) Increase in various malignant tumors (18 exposed vs 5 controls) in certain strain of rats, exposed to 2450 MHz pulsed, modulated at 8 HZ, SARs .4 to .15W/kg - frequency at power level readings similar to cell phone emissions. They also found 7 to 1 increase in pheochromocytoma tumors for exposed vs controls. The authors negated their positive findings by reinterpreting their conclusions to fit their desired outcomes. They concluded the observations as biologically insignificant due to the lack of an increase in any one malignant tumor type. *"In Vivo 2450 MHz exposure in standard rat 2-year bioassay"* Chou CK, Guy AW, Kunz LL, Johnson RB, Crowley JJ, Krupp JH,, Bioelectromagnetics **(1992)** 13:469-496; Bioelectromagnetics (1984) 5:389-398; USAF Report USAFSAM-TR-83-17 (volume 1 - Design, Facilities & Procedures); **United States Air Force Report [98]**

Electrical Occupations and Neurodegenerative Disease Trends

Epidemiology

Parkinsons, Alzheimers Dementia | occupational relationship & electrical exposrs | worker population

42) A US epidemiological study observed a hypothesized excess of neurodegnerative diseases; Parkinsons, Alzheimer's, Dementia was associated with a variety of occupations; teachers, clergy, veterinarians, hairdressers, as well as those working with 60 Hz magnetic fields and welders. *"Potential occupational risks for neurodegenerative diseases"*; Park RM, Schulte PA, Bowman JD, Walker JT, Bondy SC, Yost MG, Touchstone JA, Dosemeci M.; Education and Information Division, National Institute for Occupational Safety and Health, MS C-15, 4676 Columbia Parkway, Cincinnati, OH 45226, **USA.;** Am J Ind Med. **2005 Jul**;48(1):63-77 **[96]**

Epidemiology

Parkinsons, ALS | electrical exposur | worker population

43) A Colorado State study evaluated relation between deaths from certain neurogenerative diseases and electrical occupations. THe study used a 3 tiered method of magnetic field exposures based on a job-exposure matrix. The study observed a positive association for Parkinson's disease – odds ratio of 1.5. ALS (Lou Gehrig's) disease was associated with electrical occupations, but not with magnetic field exposure – odds ratio of 2.3. No consistent associations with magnetic fields were observed for Alzheimer's disease. *"Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases."*; Noonan CW, Reif JS, Yost M, Touchstone J ; Department of Environmental Health, Colorado State University, **United States.**; Scand J Work Environ Health. **2002** Feb;28(1):42-8 **[95]**

Epidemiology

Alzheimers, ALS | ELF electrical exposur | worker population

44) A Swedish epidemiological study evaluated the relation between extremely low frequency magnetic fields (ELF – powerline frequency) from occupational exposures and mortality from neurodegenerative diseases. The study found an increased risk of Alzheimer's and ALS but no evidence of risk was seen for Parkinson's disease or multiple sclerosis. *"Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields";* Hakansson N, Gustavsson P, Johansen C, Floderus B.; Institute of Environmental Medicine, Karolinska Institutet, Stockholm, **Sweden.;** Institute of Environmental Medicine, Karolinska Institutet, Stockholm, **Sweden. [97]**

Plants and Wildlife

In Vitro

Plant chlorophyll affected in lab RF frequency plant leaves

45) Chlorophylls were studied in the leaves of black locust (Robinia pseudoacacia L.) seedlings exposed to electromagnetic fields of low power density 400 MHz frequencies. Chorophyll levels decreased for 1, 3 and 8 hour exposure times for 3 weeks, and were enhanced for 2 hour exposure times.
A preliminary study on ultra high frequency electromagnetic fields effect on black locust chlorophylls; Sandu DD, Goiceanu IC, Ispas A, Creanga I, Miclaus S, Creanga DE.
Faculty of Physics, "Al I Cuza" University, 6600 lasi.; Acta Biol Hung. **2005**;56(1-2):109-17, **Hungary [101]**

Reviews of the Scientific Literature on RF/MW

View Point

The authors in this review of the scientific literature claim that the connection between RF radiation and adverse health effects is limited. However, they admit that there is a lack of RF studies examining the long term, low level effects of this radiation on health. They call for more of these types of studies to truly understand correlation of long term exposure.
"Health risks of electromagnetic fields. Part II: Evaluation and assessment of radio frequency radiation"; Habash RW, Brodsky LM, Leiss W, Krewski D, Repacholi M.; McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, Ottawa, Ontario, **Canada;** Jrnl - Crit Rev Biomed Eng. **2003**;31(3):197-254. [11]

View Point
This paper gives an overview of present scientific knowledge in health research at RF/MW levels to which the general population is typically exposed. The paper claims that long term studies suffer from weak methodologies and are few in number, however the authors support the validity of laboratory human experimental, short term exposure studies which reveal demonstrated biological changes by RF/MW radiation. The authors of this paper conclude "because of the present fragmentary scientific database, a **precautionary approach** when dealing with radio and microwave frequency radiation is recommended for the individual and the general population".
[Article in German] *"Radio and microwave frequency radiation and health--an analysis of the literature";* Roosli M, Rapp R, Braun-Fahrlander C.; Institut fur Sozial- und Praventivmedizin der Universitat Basel, **Switzerland.**: Jrnl - Gesundheitswesen. **2003** Jun;65(6):378-92 [16]

View Point
The article presents new literature on the biological effects of RF electromagnetic fields, and explains the cellular and biological interactions occurring during RF/MW exposures. [Abstract does not go into great detail about what they found – need the complete study]

"Biologic effects and health consequences of low and high (radio) frequency electromagnetic fields." ; Srebro Z, Dziobek K.; Folia Med Cracov. **2003**;44(1-2):201-5., **Poland** [33]

View Point
The article discusses the lack of knowledge by the medical profession in recognizing RF/ MicroWave radiation overexposure symptoms, and points out how to identify those symptoms based on today's standards. [Abstract does not point out the identifying markers] .*"Medical aspects of radiofrequency radiation overexposure";* Health Phys **2002** Mar;82(3):387-91, **USA** [51]

View Point
The article is critical of current national and international measurement parameters used to establish safety standards for EMFs from all frequency ranges. It believes the use of SARs (specific absorption rates) is a deficient measurement parameter. The authors support the use of parameters that identify electromagnetic interaction with different cellular functions such as DNA responses.
"Comment: a biological guide for electromagnetic safety: the stress response."; Blank M, Goodman R ; Department of Physiology, Columbia University, New York, New York 10032, **USA.** ; Jrnl – Bioelectromagnetics. **2004 Dec**;25(8):642-6; discussion 647-8. [55]

View Point
A scientist who tends to side with industry, believes more studies are needed to validate various past epidemiological and cellular studies that find links between cancer and cellular damage by EMRadiation from RF/ and Microwave frequencies. This is a different stance from that taken by industry scientists who announced in 2004 that there is no effect from electro magnetic radiation at current wireless communication levels. *"Mobile phones, mobile phone base stations and cancer: a review."*; Moulder JE, Foster KR, Erdreich LS, McNamee JP. ; Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI 53226, **USA.**; Jrnl - Int J Radiat Biol. **2005 Mar**;81(3):189-203 [53]

View Point
A spokesman for the larger military/industrial scientific RF/MW community demonstrates a reversal and admits that research on man has been limited to thermal reactions by RF/MW radiation. More research is needed examining human perception from a variety of RF parameters. *"Behavioral and cognitive effects of microwave exposure"*; D'Andrea JA, Adair ER, de Lorge JO; Naval Health Research Center Detachment, Brooks City-Base, **Texas, USA** Bioelectromagnetics. **2003**; Suppl 6:S39-62.[69]

Hypothesis
The paper demonstrates inadequacy of RF/MW observation-criteria in lab sleep study procedures. RF/MW lab research is limited to single-channel frequencies procedures rather than real world RF broadband exposures. Results also show that simple sleep monitoring systems based on single-channel EEG analysis, without access to the brain's original biosignals, are not adequate for sleep studies. [Article in German]
"Investigation of sleep disorders in the vicinity of high frequency transmitters"; Leitgeb N, Schrottner J, Cech R, Kerbl R.; Institut fur Krankenhaustechnik, Technische Universitat Graz.; Jrnl - Biomed Tech Berlin, **Germany. 2004** Aug;49(7-8):186-93. [18]

In-Line Wired Noise Filter for TED5000

In-Line Wired Noise Filter

$18.00 USD

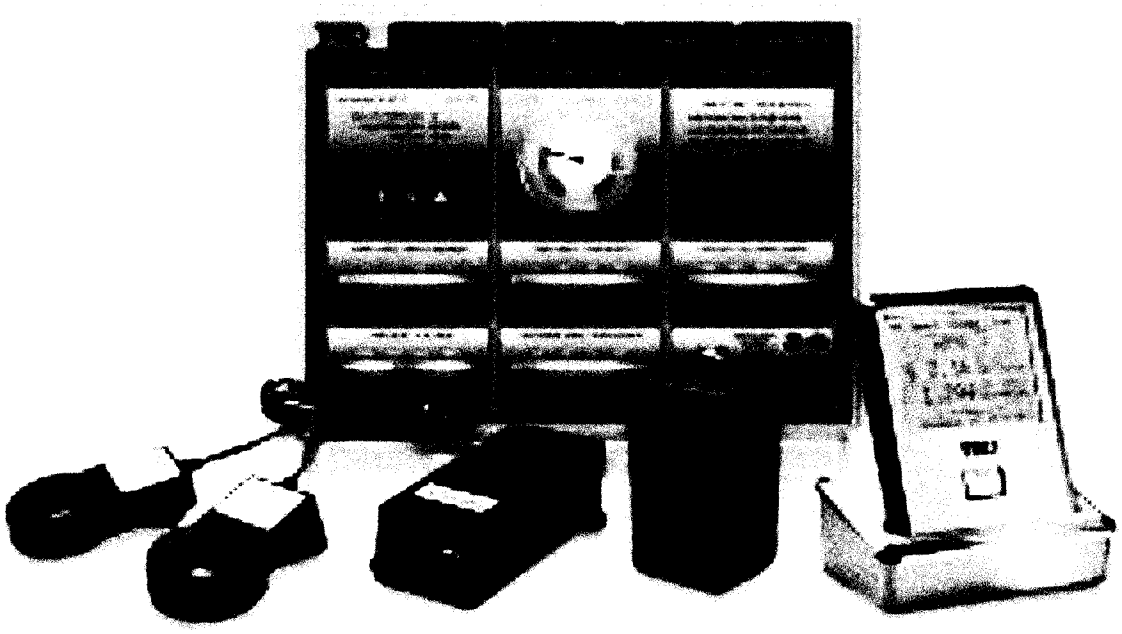
The TED In-Line Wired Noise Filter is a very useful component that can be used to isolate the MTU and Gateway in your home/office.

For example, if you have found that a circuit(s) has line-noise and is interfering with the TED-signal, this filter will isolate the MTU and Gateway so that the signal is clear of noise.

Installs in the breaker panel. Installation Guide:

- Locate the outlet you will have the Gateway plugged in. Determine which circuit breaker controls that particular outlet.
- Open the circuit breaker panel. Locate the breaker that controls the outlet in #1 above.
- Turn off, and remove the breaker from the panel.
- Remove the conductor (attached wire) from the breaker.
- Using a wire-nut, connect the BLACK wire of the filter with the black wire of the MTU and the black conductor you just removed from the circuit breaker.
- Connect the RED wire of the filter into the breaker.
- Connect the WHITE wire of the filter to the neutral bus.
- The red wire of the MTU is not used in this scenario, so cap it off with a wire-nut.
- Replace the breaker in the panel.
- Turn the breaker on.

NOTE: *You will need to adjust the System Setting configuration for the MTU (under SYSTEM LAYOUT tab) to reflect 120v (BK-WH) connection.*



Product Videos

The Energy Detective

View all The Energy Detective products

The Energy Detective TED 5000 Home Energy Monitor

A home energy use monitor which installs at your main electrical panel and measures the amount of power used within the home.

5000-C

TED 5000 - with software & local display

$239.95

The Energy Detective TED5000 Home Electricity Monitor Kits

What is TED?

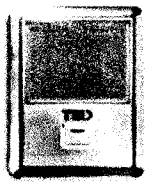
When you want to lose weight, you track your changes with a scale. When you ride in a taxi, you monitor your ride with the taxi meter. When you want to track electricity, you save with The Energy Detective (TED). TED is an in-home electricity monitor that provides real-time data in an easy-to-understand manner. TED permanently installs in your breaker panel and gives you instant feedback on your electricity usage.

How Does TED Work?

TED quickly and easily installs in your home's breaker panel. By connecting two sensor clamps around the incoming power conductors that feed your panel, TED measures the flow of electricity within your home. Information is sent over existing electrical wiring in the home to the compact wall-plug Gateway. You can then view real-time data on the wireless display or via a computer and/or smartphone.

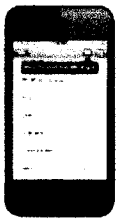
How Does TED Save?

The Energy Detective has a variety of features to help consumers save electricity around the home.



Wireless Display

Use the optional wireless handheld display (available with all "C-model" units) to instantly discover phantom loads, check usage of individual appliances, and see the difference turning a switch on/off really makes. Instantly and conveniently view real-time electricity usage, voltage, and your projected monthly bill.



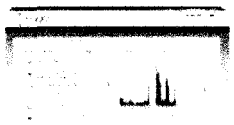
Text/Email Alerts

Use TED Advisor, a Footprints Software-based program that allows you to receive instant text message/email alerts, based on user-defined parameters. Whether you want to receive one text message a month when you are about to exceed your

budget, or a daily text message stating your highest voltage reading for the day, you have the power to set what you want, when you want it.

Footprints Software

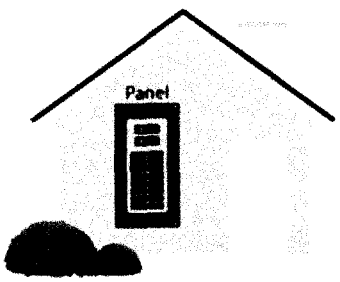
Use TED's interactive Footprints Software (embedded in all TED units) to chart and graph usage, view historical data and trends, set up TED Advisor text messaging/e-mail alerts, enter local utility-rate information, and create load profiles for individual appliances. Easily export data!

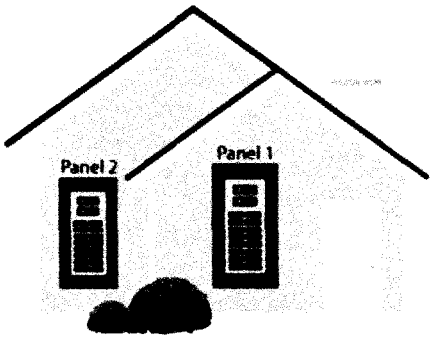


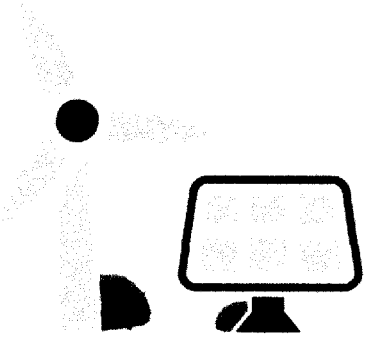
Third Party Applications

Use one of TED's third-party apps to view real-time electricity data remotely. View interactive charts and graphs, set alerts, and receive instant data on your computer/laptop, iPhone, iPad, Android, Blackberry, and other Internet-enabled devices.

Which TED is Right For You?



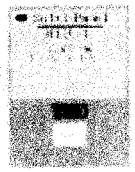




Start by determining how many sources you'll be monitoring:

I HAVE

SOURCE



b **TED 5000-G**

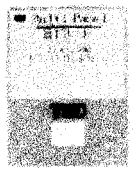
Perfect for Homes With:

- 1 electrical panel

*Wireless display included with the **TED 5000-C***

I HAVE

SOURCES



TED 5003-G

Perfect for Homes With:

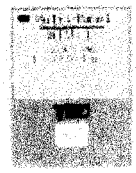
- 1 panel & 2 subpanels
- 2 panels & 1 subpanel
- 3 panels
- 1 panel & 2 wind/solar power
- 2 panels & 1 wind/solar power

*Wireless display included with the **TED 5003-C***

I HAVE

2

SOURCES



TED 5002-G

Perfect for Homes With:

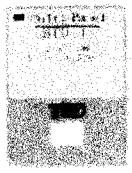
- 1 panel & 1 subpanel
- 2 panels
- 1 panel & 1 wind/solar power

*Wireless display included with the **TED 5002-C***

I HAVE

3

SOURCES



TED 5004-G

Perfect for Homes With:

- 1 panel & 3 subpanels
- 2 panels & 2 subpanels
- 4 panels
- 1 panel & 3 wind/solar power
- 2 panel & 2 wind/solar power
- 3 panels & 1 wind/solar power

*Wireless display included with the **TED 5004-C***

TED 5000 Key Features

Instant Text/Email Alerts

Want to receive an alert as soon as your rate changes, or if you're getting close to your budget? Receive instant email/text message alerts with TED Advisor. Simply set your customized parameter(s) in TED's Footprints Software and receive alerts as often as you'd like!

View Data Remotely

Want to view electricity data for a vacation home, or while you're on the go? TED allows you to view data on your home computer and/or on an optional wireless Display. And, if you have Internet service, you can view data on any Internet-enabled device with one of our third party apps.

Monitor Individual Appliances

Want to monitor an individual appliance, such as your HVAC or Hot Water Heater? TED's Load Profile Wizard is a software-based program that learns how much electricity an appliance uses when it's off/on. TED will track up to five individual appliances and provide you daily total usage, and associated costs.

Easily Export Data

Want to export and store your data to share with others, or to create your own charts and graphs? Even though TED stores up to 10 years of data, you can instantly export -Second, -Minute, -Hour, -Day, and Month-data to a CSV (Excel) file at any time.

Monthly Bill Projection

Want to have an accurate estimate of what your electricity bill will be this month? TED's intuitive Utility Setup Wizard allows you to enter your own utility rate structure, resulting in a very accurate bill projection.

Interactive Charts and Graphs

Want to receive accurate data on your electricity usage, CO2 emissions, and voltage readings? TED provides data updates every second, with a sensitivity of one-watt and +/- 2% accuracy. TED's interactive Footprints Software creates real-time charts and graphs to help you visualize data and see trends.

bbbb

- Intuitive, simple setup directly from Computer
- Compatible with Windows PC, Mac & Linux
- Wireless hand-held display (optional)
- Backlit display (optional)
- Rechargeable Battery - no batteries to change
- Accurate to within 2%
- User can customize displays
- Adjustable sensitivity - user can adjust down to ONE WATT
- View real-time energy data remotely via Internet or mobile device
- Optional Solar/Wind Package - Net-Metering capability
- Receives signal from multiple sources
- Ties into Home Automation Systems
- Stores detailed data for export to computer
- Accommodates all rate structures - flat, tiered, time-of-use, demand, seasonal (4 seasons), weekend/holiday, or any mix of structures!
- ANSI/UL (1244) Approved
- CAN/CSA (C22.2) Approved

TED 5000 Software

There are a variety of Third-Party Applications for both PC and Mobile Devices that allow you to plot and analyze the data from your TED-5000

TED Footprints Software

Use TED's interactive Footprints Software (embedded in all TED units) to chart and graph usage, view historical data and trends, set up TED Advisor text messaging/e-mail alerts, enter local utility-rate information, and create load profiles for individual appliances. Easily export data!

View a Live Demo Here

Mobile Apps:

TED-O-Meter

is a free smart phone application that is compatible with iPhone and iPod Touch. An interactive dial shows real-time electricity usage.

People Power 1.0

is a free energy manager app available for Smartphones that provides real-time insight, choice, and control over household energy use. It integrates with the TED 5000 Gateway™ through a simple set-up and connects to People Power's analysis software to deliver useful information anytime, anywhere.

MiraWatt T5K

allows you to view power usage data on your iPhone. A simple swipe gesture on your iPhone will change the view from Hour, Day, Week, etc.

---

iTED

is a mobile application for iOS and Android OS devices such as the iPhone and Droid phone models for monitoring energy usage in conjunction with our TED 5000 series. You can monitor your home and or business energy usage while-on-the-go or the help figure out about how much that new appliance you turned on uses in energy!

TED 5000

is a free mobile application for the iPhone that provides current Power and Cost, as well as average power and cost for the billing cycle. The user can refresh their energy data anytime by clicking the refresh button.

---

andTED

is an energy monitoring application for TED 5000 users on Android. This application allows you to view MTUs independently, which is great for consumers with solar or wind installations.

TEDisplay

is a mobile application for HP/Palm webOS devices, such as the Palm Pre and the Palm Pixi. TEDisplay works with your TED 5000 to monitor energy usage directly on your phone. TEDisplay supports multi-MTU configurations with access to just about every data value available from the TED 5000. And, with a properly configured home network, you can monitor your energy usage from just about anywhere!

Desktop Applications

Bidgely

Is a free cloud based energy monitoring and management tool. Features interactive graphs that show real time energy use. View individual appliance energy consumption, simple pie charts show appliance-level breakdown of energy bill. No additional hardware plug level sensors required. Provides personalized recommendations on saving money. Features timely alerts that avoid unexpected high energy bills.

PlotWatt

Is a free application that features cloud-based algorithms to analyze your TED data and provide appliance-level insight, feedback and recommendations to help save money on your electric bills.

Reduce electricity usage by up to 50%. Recieve custoimized money-saving recommendations and tips. PlotWatt Energy Dashboard consolidates energy information. Electricity usage presented in an easy-to-understand format.

MyEragy

Available in both Free and Pro versions, MyEragy is an electricity monitoring platform that allows homeowners to check the details of their energy consumption to best understand how they can reduce their electricity bills.

Easily monitor energy generated by solar, wind, and gas generators. Eragy's proprietary Utility Rate Engine helps users understand rates. Email and text/SMS alerts including usage and cost budget overruns. Set rate alerts such as when a rate tier is about to be exceeded.

People Power 1.0

A free intelligent iPhone and Android Smartphone application that helps manage your personal energy use to save money.

Set daily and monthly budgets, along with alarm alerts. Compare energy usage with others in your area. Take energy quizzes to learn how to save more electricity. Post Facebook updates with your electricity usage. View accurate projections of monthly bills.

it's electric

One of the first free applications that allows you to view tour TED 5000 electricity data remotely on the web. Shows detailed historical data with different resolutions. View interactive graphs and locate energy hogs. See instant updates while you explore your usage.

TED the Toolbar

TED the Toolbar is a Firefox only toolbar that allows you to view real-time energy data from your TED system while you surf the Web. Shows historical data and projected monthly bill. View graphs on electricity usage for detailed data. See instant updates on the top of the page while you surf the web.

Popular Accessories

Click on a category to view a selection of the most popular accessories compatible with the The Energy Detective TED 5000 Home Energy Monitor.

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

We can't shut off meters!

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?

Your AntennaSearch Report is ready!

1200 W Washington St, Phoenix, AZ 85007

- Results Summary - Dec 12, 2014 -

Search Radius reduced to 3.0 miles
(High number of Antennas Detected!)

107 Tower Structures Detected!

2 New Tower Applications Detected as of 12/12/14!

857 Antenna Locations Found!

TOWER - Towers are tall structures (typically over 200 ft) used for Cellular, Paging and other radios services. Towers can contain multiple antennas owned by various companies.

Alert! 107 Towers (18 Registered, **89 Not Registered**) found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Tower is .37 miles away and is owned by **Spectrasite Communications, Llc. Through American Towers, Llc.**.

Alert! 2 New Tower Applications found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

ANTENNA Antennas are the actual signal emitters for cellular, paging and other radio services. Antennas can be placed on towers or be stand alone and placed on top of offices, condos, churches, light poles, signs, etc. Stand alone Antennas are small and difficult to spot as they are easily hidden/camouflaged.

Alert! 857 Antennas found within 3.00 miles of **1200 W Washington St, Phoenix, AZ 85007**.

Info! The NEAREST Antenna is .14 miles away and is owned by **Central Arizona Shelter Services**.

This Website search revealed that you have 857 Antennas within 3.0 miles. It revealed you have 107 towers within 3.0 miles and 89 of these are not registered. This Website may or may not be up to date, but has verified the above information to its best knowledge.

Is this acceptable to you? Do you realize how out of hand this really is?