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Health Effects of Mobile Phone Usage

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ABSTRACT

Uncertainty about the association between health risks and exposure to radiofrequency radiation emitted by cellular and cordless mobile phones can be addressed by a critical analysis of the methodology used in studies assessing this relationship. Studies funded by cellphone companies give reassuring conclusions but are affected by biases and flaws, whereas public-funded studies are without these errors and show acute and chronic effects, including head tumors, findings supported by biological evidence.

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INTRODUCTION

We provide an overview of the relationship between exposure to cellular and cordless phone radiofrequencies and possible health effects. One key concern is the large disparity between the results from public- and from private-funded research. Drawing on Tomatis (2005), founder and long-serving (1969-1993) head of International Agency for Research on Cancer (IARC), the method used in many private-funded studies is such as to raise background noise, increasing confusion, thereby making assessment of risk more difficult. It is thus important to critically assess the scientific validity of these studies: a crucial point we raise is the conflicts of interest often affecting the parties involved, whether individual scientists, international journals, or safety agencies. The implications are far reaching, going beyond the lack of awareness in mobile phone (MP) users regarding health risks, and limited insight on potential improvements due to failures in scientific research. The prime consequence is that collective decisions concerning how these devices should be produced and made available are precluded by the fallacious scientific knowledge that vested interests explicitly pursue.

A pioneer study exposing carcinogenic risk arising from MP use was published by Hardell (Hardell et al., 2002) of the Dept Oncology, University Hospital, Orebro, Sweden. This seminal work has now been extended by a number of notable authors: Davis (Davis, 2010) of the Environmental Health Trust, Tetom Village, WY USA; Gee (Gee, 2009) at the European Environment Agency, Copenhagen, Denmark; Lloyd Morgan (Lloyd Morgan, 2009) in Albany, CA USA; Kundi (Kundi, 2009) at the Environmental Health Institute, University of Vienna, Austria. In addition, one of the present authors, Levis (Levis et al., 2011), has worked in this field for more than 10 years, and has frequently been called as an expert witness to give evidence in the context of MP court cases.

Investigators in newer areas of research, tackling the increasing challenges of acute and chronic effects of electrohypersensitivity, include Johansson (Johansson, 2006) at the Karolinska Institute and Royal Institute of Technology, Stockholm, Sweden; Khurana (Khurana, 2010) at the Australian National University Medical School, Garran, Australia;

and Grigoriev (Grigoriev 2011) at the Federal Medical Biophysical Center, Moscow, Russia.

OVERVIEW

According to the International Telecommunications Union, by the end of 2013 the number of cellphone subscriptions reached 6.8 billion, with 4.4 billion users, half being children and young adults. There are no data for cordless phones, but 3 billion users is a reasonable assumption. Given these figures, even a modest increase (20%) in tumor risk for MP users would result in significant social costs, while higher risks could lead to a crisis of dramatic proportions. While most technologies carry risks, these should be assessed accurately and responsibly. Whether or not there is a relationship between MP use and head tumor risk is still under debate: progress requires a critical analysis of the methodological elements essential to any impartial evaluation of contradictory results.

CURRENT SCIENTIFIC KNOWLEDGE

MPs were introduced onto the market in the 1980s, and widely used during the following decade in the USA, Scandinavia and Israel. From the early 1990s MP use spread quickly in other countries, with a resulting almost global exposure to MP radiation for >20 years. Although head tumors may have very long latency times (even 30 years or more), it is likely that some due to MPs could be diagnosed after ≥ 10 years of use or latency, as in the case for long-latency tumors due to ionizing radiation, asbestos or smoking. Studies by the same author (Hardell, Carlberg & Hansson-Mild, 2006a,b; Hardell, Carlberg, Soderqvist & Hansson-Mild, 2013a,b) as well as other authors (Han, Kano, Davis, Niranjana & Lunsford, 2009; Khurana, Teo, Kundi, Hardell & Carlberg, 2009; Dubey, Hanmandlu & Gupta, 2010; Sato, Akiba, Kubo & Yamaguchi, 2011; Coureau et al., 2014), report a statistically significant (s.s.) increase (from >100% to >300%) in risk of ipsilateral malignant (gliomas) and benign (meningiomas) cerebral tumors, and of benign acoustic-nerve tumors (neuromas) among MP users, after use or latency ≥ 10 years. Moreover, the increase in annual incidence of brain and nervous-system tumors was correlated with potential confounders and environmental risk factors in over 100 countries using ecological data: the

only exogenous risk factor consistently associated with higher incidence was penetration of MP subscription rate (De Vocht, Hannam, & Buchan, 2013; Hardell & Carlberg, 2013). Instead, several researchers have drawn their own conclusions from the results of the Interphone studies, which involved research groups from 13 countries (Interphone Study Group, 2010, 2011) and are considered reassuring in their failure to find any increased risk of head tumors in MP users. It is therefore vital to understand the weight of the conflicting data here.

We carried out a critical examination of the protocols and results from all epidemiological case-control and cohort studies, pooled analyses, and meta-analyses on head tumor risk among MP users (Levis, Minicuci, Ricci, Gennaro & Garbisa, 2011, 2012). For each study we identified the elements that should be taken into account to ensure impartial evaluation of reliability (Box 1):

BOX 1 *Methodological elements needed to ensure the reliability of studies on the relationship between MP use & increased head tumor risk*

- frequency of MP use and compatibility of latency and/or exposure time since first use of MPs with progression time of the examined tumors;
- inclusion among the exposed of all users of MPs, cordless included;
- laterality of head tumor localization relative to the habitual laterality of MP use;
- percentage of actually exposed subjects, number of subjects selected (cases and controls), and percentage of their participation in the study;
- distribution of risk values above and below 1, and probability that such distribution might be chance;
- full and correct selection and citation of data included in the meta-analyses.

Basing our assessment on these elements we identified several study design flaws and biases that lead to underestimation of tumor risk in the Interphone studies funded by the cellphone companies, which are absent in Hardell's public-funded work (Box 2).

BOX 2 *Methodology errors in the Interphone negative studies, based on a "non-blind" protocol; reliability of Hardell positive studies, based on a "double-blind" protocol*

Interphone

- inadequacy of "regular use of cell phones" defined as "at least 1 phone call/week, for at least 6 months": 2-5 min/day, often for <5 years;
- inadequate exposure or latency time in relation to time required for diagnosing the tumors concerned: fewer than 5% of cases have latency time ≥ 10 years;
- fails to include cordless users, subjects younger than 30, and people living in rural areas, even though these groups have high exposure;
- fails to distinguish tumor laterality in relation to laterality of MP-use;
- fails to consider other types of malignant and benign head tumor, except for astrocytomas, neuromas, meningiomas and salivary gland tumors (1 study);
- participation of controls is reduced to 60%, at times <40%, with prevalence of the exposed;
- the patient, interviewed face-to-face when in a confused state during the post-operative period, may report the recent laterality of use which, as a result of the disturbances brought about by the tumor, may not be the side habitually used before tumor development;
- the negative findings are publicized as fully reassuring even though these at times include positive data indicative of increased carcinogenic risk, e.g. for only ipsilateral tumors, or only in the subgroup exposed for ≥ 10 years, or only in residents in rural areas.

Hardell

- MP use is significant: from over 16 to over 32 min/day, for ≥ 10 years;
- 18% of cases were exposed for or from ≥ 10 -15 years;
- includes them;
- tumor laterality is always considered in relation to MP-use laterality;
- other types of head tumor are considered separately;
- exposed and non-exposed controls participate in equal proportion and at high percentage (nearly 90%);
- the data are collected through a questionnaire sent to cases on dismissal from hospital, when they are recovering;
- the currently positive findings are correctly examined.

Studies funded by public bodies, without flaws or financial conditioning, point to cause-effect relationships supported by biological plausibility (Box 3).

BOX 3 *Non-thermal effects of RF supporting the biological plausibility of possible harm to health from this radiation*

- inhibition of synthesis of hormone melatonin, involved in deactivation of peroxide radicals which produce DNA damage triggering carcinogenesis;
- stimulation of Fenton's reaction, with consequent increase in damage due to free radicals on biological macromolecules;
- modification of cell membrane permeability and consequent alteration of flow of biologically important ions;
- modification of brain's electrical activity and of permeability of hemato-encephalic membrane, with consequent damage to cerebral neurons and alteration of functioning of cerebral neuroreceptors and neurotransmitters;
- alteration of immune system functioning;
- inhibition of apoptosis (programmed cell death);
- expression of heat shock proteins;
- genetic and epigenetic effects;
- synergistic interactions with well known carcinogens.

The Interphone data have been publicized as reassuring by their authors as well as by the organizations promoting and funding the work [IARC and European Union (EU): 70%; cellphone companies: 30%], by many agencies responsible for protecting human health, and by over 100 newspapers in their headlines worldwide. This 'acquittal' of MP-use flew in the face of a 'commentary' by Saracci, member of the Working Group Secretariat, and Samet, Chair of the IARC Working Group on radiofrequencies (RF), which bore a telling title: "Call me on my mobile phone...or better not? – a look at the Interphone study results" (Saracci & Samet, 2010). This article highlighted the various major defects of the Interphone protocol that would have substantially 'diluted' risk estimates. And a further publication raising concern came in an editorial by Cardis (Interphone coordinator and member of the IARC Working Group on RF) and Sadetzki (Israeli Interphone team head),

entitled: "Indications of possible brain-tumor risk in mobile-phone studies: should we be concerned?" (Cardis & Sadetski, 2011), showing that the only Interphone data that actually used the factors essential for identifying a carcinogenic effect due to cell phone exposure (significant time use, continuity of use or latency of ≥ 10 years and ipsilateral tumor detection) gave rise to s.s. increases ($>100\%$) of glioma, acoustic neuroma and parotid gland tumor risks. As they stated: "The overall balance of the above-mentioned arguments suggests the existence of a possible association". Additional factors contributing to dilution of risk estimates, not reported in these editorials, are pointed out in our recent articles (Levis & Gennaro, 2012; Levis, Gennaro & Garbisa, 2012) (Box 2).

The conclusive report by the IARC Working Group on RF evaluated the Interphone data as follows (IARC, 2011): "There was suggestion of an increased risk for ipsilateral exposure... and for tumours in the temporal lobe, where RF exposure is highest. The risk for glioma increased with increasing RF dose for exposures 7 years or more before diagnosis, whereas there was no association with estimated dose for exposures less than 7 years before diagnosis". And regarding Hardell's data: "A Swedish research group did a pooled analysis of two very similar studies of associations between mobile and cordless phone use and glioma, acoustic neuroma, and meningioma. The risk for glioma increased with increasing time since first use and with total call time, reaching 3.2 s.s. for more than 2000 h of use. Ipsilateral use of the MP was associated with higher risk. Similar findings were reported for use of cordless phones". The report concludes: "Although both the Interphone study and the Swedish pooled analysis are susceptible to bias, the Working Group concluded that the findings could not be dismissed as reflecting bias alone, and that a causal interpretation between MP exposure and glioma is possible. A similar conclusion was drawn from these two studies for acoustic neuroma, although the case numbers were substantially smaller than for glioma. Additionally, a study from Japan found some evidence of an increased risk for acoustic neuroma associated with ipsilateral MP use" (Sato, Akiba, Kubo & Yamaguchi, 2011). The Working Group classified RF as "possible carcinogenic agents for men" (group 2B), but an evaluation of higher risk, i.e., as "probable carcinogenic

agents for men” (group 2B), was sustained by a minority group of the Working Group (IARC, 2011, 2013).

According to Samet: “The evidence, while still accumulating, is strong enough to support a conclusion and the 2B classification. The conclusion means that there could be some risk, and therefore we need to keep a close watch for a link between cellphone and cancer risk.” Moreover, according to Wild, IARC Director: “Given the potential consequences for public health of this classification and findings, it is important that additional research be conducted into the long-term heavy use of MPs. Pending the availability of such information, it is important to take pragmatic measures to reduce exposure, such as hands-free devices or texting.” (IARC, 2011).

IARC is an international scientific organization operating under the aegis of the World Health Organization (WHO). Tomatis (2002), head of IARC, and Huff (2002), editor of IARC Monographs (1977-1979), warn that from 1994 IARC has witnessed a complete overhaul of the criteria for evaluating carcinogenicity, with a wholesale devaluation of the criteria underpinning identification of carcinogenic factors: 1) the criteria for evaluating an agent’s carcinogenicity, based on study of the mechanisms of action (biological effects, in particular genotoxic), are no longer applied; 2) the evidence of carcinogenicity deriving from animal experimentation is undervalued; 3) possible confounding factors of the scientific criteria aimed at primary prevention of carcinogens in the workplace or home are highlighted out of all proportion; 4) consequently, epidemiological data are rarely conclusive; 5) a higher percentage (from <10% in the 70s to >30% in the 90s) of experts open to influence by conflicts of interest are being invited by IARC onto the Working Groups. As a result, according to Tomatis and Huff, the IARC Monographs have lost their initial authority and independence.

This criticism can easily be leveled at the RF Working Group because >65% of its members were affected by conflicts of interest; two (Ahlbom, appointed Working Group Chairman, and Lerchl), though invited, were not even able to participate owing to the disclosure of their conflicts of interest (IARC, 2011, 2013; Levis, Gennaro & Garbisa, 2012).

The discrepancy between the Interphone and Hardell data is highlighted by a meta-analysis of 24 case-control studies. This work (Myung et al., 2009) observed a s.s. positive association between MP use and increased head cancer risk in 10 "high-quality studies" (7 by Hardell, only 1 by Interphone, 2 by other groups), but a negative association indicating an apparent protective effect in 14 "low-quality studies" (12 by Interphone, 2 by other groups, none by Hardell). The authors reach the following conclusion: "We feel the need to mention the funding sources for each research group because it is possible that these may have influenced the respective study designs and results". While, as noted, Hardell's work was only public-funded, the Interphone studies received financial support not only from the EU and IARC, but also from the Mobile Manufacturers Forum (an umbrella body for the 12 international MP industries), the Global System for Mobile Communication Association (another strong lobby of the MP industries), and the Wi-Fi Alliance, which brings together the many industries involved in the uptake of new technologies and wireless services: there are 309 listed on its website. Moreover, Interphone authors received additional funding from their national MP companies (Box 4).

BOX 4 *Number of studies funded by national MP companies*

- 7 Mobile Telecommunications Health and Research
- 2 AFA Insurance, TeliaSonera, Telenor, Ericsson and ZonMw
- 7 German Mobile Phone Research Program
- 2 Finnish National Technology Agency
- 4 Canadian Wireless Telecommunications Association
- 6 French Orange, SFR and Bouygues Télécom
- 5 France Télécom
- 2 Telstra Australia
- 6 UK Vodafone, O2, Orange, T-Mobile, "3", and Scottish Executive
- 3 Intn. Epidem. Inst. (Rockville, MD USA), private MP-company consulting body

Even so, of the Interphone authors 18 fail to make any declaration about conflicts of interest, 13 state “conflicts of interest: none declared” (whether stated by the authors or the editor is unclear), while only 7 “declare any conflicts of interest” (Levis & Gennaro, 2012; Levis, Gennaro & Garbisa, 2012; Levis, Minicuci, Ricci, Gennaro & Garbisa, 2011).

The consequences of the cellphone-company funding on the methodological design of the Interphone Study, its results and interpretation have been denounced by other authors [BioInitiative, 2012; European Environment Agency (EEA), 2008; Hardell, Carlberg & Hansson-Mild, 2008, 2011a; Radiation Research Org., 2009; Kundi, 2009; Havas, 2010; Davis et al., 2013].

One example, a review by an Indian research group (Dubey, Hammandlu & Gupta, 2010) on the use of mobile telephony and head tumor risk, concludes: “Interphone ... a nonblinded, interview-based, substantially wireless industry-funded case-control study ... has been reporting highly questionable results in comparison with the independent studies”, whereas “Hardell’s studies have reported a link of brain tumor risk from cell phone use and cordless phone use.... These studies had no industry funding and are entirely independently funded”. The authors add: “A study discovered remarkable differences between the independent research and the industry-funded research in favor of industry interests. By falsifying the evidence, the latter showed that the radiation could protect against tumors” (see Fig.2 of their paper).

Even the evaluations of falsely reassuring results by some of the major national and international organizations are compromised by conflicts of interest. According to Tomatis (2005), the method used was the careful and systematic production of results, both experimental and epidemiological, whose sole purpose is to raise the background noise, increasing confusion and thereby making correct assessment of risk more difficult because the best way to halt, or at least delay, a decision of public health issues is to inject doubts about the validity of data that are uncomfortably positive. For instance, Hardell reports (Hardell, Walker, Walhjalt, Friedman, & Richter, 2006) that: in 2001, of 1386 scientific articles, 16% were funded privately; by 2004 the number of articles funded privately had

increased to 33%; in 2004, 25% of articles published in two of the world's leading biomedical journals were signed by at least one author with conflicts of interest. Hardell comments: "These data are an underestimate owing to the accepted and now widespread custom in many journals not to indicate – or to indicate only partially – the sources of funding for the work carried out. This state of affairs means that information produced by independent research on the environmental and health risks has almost no influence".

Furthermore, in an interview published in July 2007 by the Association 'Liberterre', G. Carlo (2007), author of the book 'Cell Phones: Invisible Hazards in the Wireless Age', stated that: 1) "while perfectly aware of the health risks inherent in EMF exposure, industry does not alter the present situation unless there is a drastic intervention from governments and agencies responsible for protection of health; 2) the 'pollution' of scientific information due to funding given by industry to researchers, agencies and governments has today reached unimaginable proportions: at least 50% of studies on the effects of RF are funded by sector industries; 3) many scientists funded by these industries have stated that the results of their research, where unfavorable to the interests of the commissioner of the work, have been modified by this latter or deleted in full; 4) the likelihood of finding a no-effect result is six times higher in studies funded by the industry companies than in those funded by public bodies; 5) industry also controls the dissemination of scientific information about the effects of RF, so also influencing the way the public perceives the dangers connected with the technologies in question".

Other significant data have been published by Huss (Huss, Egger, Hug, Huwiler-Muntener, & Roosli, 2007), who selected particularly important articles about the biological and health effects of RF: if one is the average probability of s.s. positive results in work funded by public bodies, the probability of at least one positive result in those funded by the cellphone companies is just one positive result out of ten. The probability for studies with mixed funding sources lies somewhere between, and even studies not citing any source of funding (increasingly common owing to lax editorial work) are influenced to some extent.

Huss concludes by recommending that “the interpretation of the results from existing and future studies of the health effects of RF radiation should take sponsorship into account”.

Our critical review of studies on the biological and health effects of RF (Levis, Gennaro & Garbisa, 2012) found that, of 1056 articles published in peer-reviewed journals, 44% reported negative results (no adverse effect), with 93% funded by either private bodies or non-specified sources. Instead, the rest reported some type of biological effect or harm to health, with 95% funded by public bodies. There is massive intervention by the private funders in testing that is expensive, long, and difficult to perform, e.g., experimental carcinogenesis on animals, genotoxicity testing predictive of possible carcinogenic effects, and epidemiological studies on head tumors in MP users. There is therefore a constant vast prevalence of negative results in studies funded by private bodies, and of positive results in those funded by public bodies, just as there is a constant almost zero probability that this difference be due to chance.

FIRST-EVER COURT RECOGNITION OF CAUSAL LINK BETWEEN MP USE AND HEAD TUMORS

A judgment (no. 614 of 10 December 2009) of the Brescia Labor Appeal Court (Italy) recognized for the first time the association between MP use and increased risk of head tumors (Levis, Gennaro & Garbisa, 2012). The case was an ipsilateral neuroma of the trigeminal nerve in a subject who had workplace exposure for >10 years, with >15,000 hours on cellular and cordless phones. This case therefore concerned a personal situation where the technical consultant appointed by the Court and the plaintiff consultants (including Levis) evaluated the pathology as a probable consequence of a causal link to the subject’s exposure to MPs. This carried weight in the decision of the Court, which recognized that “it is likely (qualified probability) that RF have a role which is at least contributory in the development of the origin of the tumor suffered by the subject”. This led to recognition of and compensation for the suffering of a physical impairment, which was evaluated 80% of the overall working ability of the subject.

This sentence from the Brescia Court has several aspects of particular interest:

- until 2008, non-ionizing EMF were included in Italian ‘tables of professional diseases’ and for any employment involving possibility of exposure; this covered an indemnity of unlimited duration for appearance of tumors. Through decree of 9 April 2008, EMF were removed from these tables. However, a deliberation of the Italian Constitutional Court had extended welfare care to include pathologies that, while omitted from the tables, were traceable to workplace exposure. Here though, the worker has the burden of demonstrating the cause-effect relationship, i.e., showing with reasonable certainty that the pathology has arisen through workplace exposure;
- the literature widely documents increased risk of acoustic neuromas in long-term MP users, while there is absence of cases showing correlation between MP exposure and increase in trigeminal tumors. In this case, as confirmed by expert witnesses, recognition of workplace disease is based on the fact that acoustic and trigeminal nerves both originate in the same delimited area of the endocranial volume (Gasser ganglion) clearly irradiated during MP use;
- there are significant discrepancies between the Interphone conclusions dismissive of possible link between MP use and increased head tumor risk, and the very alarming findings of Hardell's group and others. But the Interphone studies are characterized by flawed experimental protocols and errors in their results and interpretation, a consequence of the influence of cellphone-company funding (business biases). Addressing the independence of available scientific studies, the Brescia Court ruled as follows: “differently from the IARC study co-financed by manufacturers of mobile phones, studies referred to by the Court-appointed expert were independent”.

The five judges of the Italian Supreme Court (Cassazione) (sentence no. 17438 of 3-12 October 2012), having carefully reconstructed the litigation track of this case, fully and definitively confirmed the Brescia sentence. As practice requires, they based their decision not on ‘merit’, already amply debated in the earlier stages of the litigation, but on ‘law’, i.e., on the correctness of the procedural aspects of the Appeal Court. Finally, the Supreme

Court decision is significant because it recognizes and confirms the importance of independence in science, in stating that “an additional and non-illogical basis of the conclusions is the further remark about the greater reliability of such studies (cited by the Appeal Court experts in favor of causation), considering their independence by virtue of not being co-financed by the mobile phone manufacturers, as distinct from other studies (cited by the defendant in denial of causation) which were.”

As regards human health and the precautionary limits on EMF exposure, the Italian judiciary at all levels and grades assumed an innovative position (Levis, Gennaro & Garbisa, 2012):

- sentence 43678/2003 of the Milan Civil Court initially referred to sentence 9893/2000 of the Italian Supreme Court, which established that the limits put forward by the international agencies and even those set by law should not be the only points of reference in controversies on possible harm to human health deriving from exposure to EMF, and that any judge presiding over a particular case has full powers, including as regards determining risk to health on the basis of scientific knowledge acquired at the time of the ruling;
- as a consequence, the Milan judge upheld the conclusions of the Court consultant, which make frequent reference to those of the plaintiff consultant Levis, and established that values above 0.6 V/m, although below the most precautionary limits set by current Italian law (6 V/m), should be considered a danger to human health;
- this principle has frequently been cited in court (up to Supreme Court) sentences for exposure to powerline EMF: here 0.2-0.3 μ Tesla must be the reference precautionary limit for new powerlines, and not the 3 μ Tesla for new lines or the 10 μ Tesla for those already in place set by Italian law for residential exposures;
- the constitutional right to health is understood in the broadest sense, including the right to live in an environment that is healthy and that should also be protected preventively, i.e., where there is the presence of merely a danger of falling ill or contracting a disease.

To be effective, this protection cannot be subordinate to a state of illness or disease arising;

- the harm (risk) should be prevented and compensated for, even if it is not known who will be affected nor when, because when it does strike it will be too late;
- observation of the limits set by law does not make EMF exposure legal and compatible with protection of right to health. Instead, account should be taken of the constitutional relevance of the right to health (Italian Constitution, Art. 32) and of the consequent level of protection, necessarily prevailing over freedom of enterprise, provided for by Constitution Article 41: "Private economic endeavor is free but may not be carried out in conflict with social utility or in any way that compromises safety, freedom or human dignity" and: "The law determines the programs and appropriate controls in such a way that public and private activity can be directed towards and coordinated for social goals";
- the scale of values set out by the Constitution should also include the Precautionary Principle, as provided for by EU Treaty Article 174, which should be considered part of national regulations;
- where there is doubt as to level of risk, the Precautionary Principle requires the adoption of the most conservative arrangement consistent with minimizing risk, where necessary opting for 'zero risk';
- where a number of epidemiological studies have shown a significant increase in risk, the emissions should be considered dangerous, even though the mechanisms of action are still unknown. Here, in fact, the causality link can only be determined in terms of probability.

ACUTE EFFECTS OF EMF ELECTROHYPERSENSITIVITY

Electrohypersensitivity (EHS) (Johansson, 2006) describes a multi-organ adverse reaction to EMF, characterized by a wide range of aspecific symptoms. These can vary with intensity and duration, and are experienced by some as a result of exposure in the workplace or home to EMF emitted by various sources, whether low or high frequency (0-

300 GHz). From the 60s, in countries of east Europe, there were reports of a new workplace disease defined as “microwave sickness” (Sadchikova, 1974; Hocking, 2001): these cases involved thousands of workers in the manufacture, inspection, repair, and maintenance of microwave equipment including radar, radio/TV station and mobile telephony. Researchers generally outline three characteristic syndromes: 1) neurological and/or asthenic: heaviness of head, fatigue, irritability, sleepiness, memory loss, and electroencephalography changes; 2) autonomic vascular changes: sweating, dermographism, blood pressure changes; 3) cardiac: heart pains and electrocardiography changes. Notably, workers exposed for periods above five years exhibited greater symptomatology. In addition, ceasing work was found to bring about a stabilization or improvement of symptoms. In the following years, researchers in western countries encountered similar cases (Glaser, 1972; Zaret, 1973).

In the 80s, Swedish neuroscientist Johansson described new symptoms, described as “screen dermatitis”, relating to video display unit operators (Johansson & Liu, 1995; Johansson et al., 2001). In addition to the nervous system and heart, the symptoms involved the skin, mainly facial, with burning sensation, itching, reddening, blisters and spots. Numerous publications by Johansson followed, describing a possible pathogenetic mechanism of action for these particular symptoms, with degranulation of the mastocytes and massive release of histamine, to the point that EHS was defined as a “functional impairment” (Johansson, 2006).

The 90s saw an exponential adoption of wireless technologies (cell phones, cordless, tablets, Wi-Fi, Wi-max, smart-meters, MP radio-base stations, etc.). With this came an increase over time of recorded occurrences of subjective symptoms relatable to EHS, also documented in many observational epidemiological studies in the home environment, in addition to the earlier workplace studies. Particularly noteworthy is the review by Khurana et al. (2010) on the neurobehavioral effects of home exposure to radiation emitted by mobile phone base stations. In the studies of Santini (Santini, Santini, Danze, Le Ruz & Seigne, 2002) in particular, and Navarro (Navarro, Segura, Portolés & Gómez-Perretta,

2003) – recently revisited by Gómez-Perretta (see below) – there appears to be a clear, significant correlation between exposure and development of symptoms attributable to EHS. For example, the correlated symptomatology is affected by distance from source, while levels of specific absorption rate (SAR) $0.11\text{--}0.01 \mu\text{W}/\text{cm}^2$ are sufficient to induce non-thermal biological/health effects (Gómez-Perretta, Navarro, Segura & Portolés, 2013). These data demonstrate that current guidelines for exposure limits (for both highest and lowest frequencies) are hardly precautionary in protecting the population from possible events adverse to health (Belyaev, 2005).

Other major sources of high frequency EMF emissions are MPs. Many studies have described adverse events in MP users: headaches, fatigue, dizziness, sleep problems, memory loss, difficulty in concentration, attention deficit, dysaesthesiae (peripheral neurological effects), tinnitus, sensation of hotness around the ears, etc. (Chia, Chia & Tan, 2000; Edelstyn & Oldershow, 2002; Al-Khalaiwi & Meo, 2004; Hillert et al., 2007; Hutter et al., 2009). Havas and Marrongelle (2010, 2013) showed effects, in controlled and repeated studies, in subjects exposed to cordless telephone frequencies of 2.4 GHz (a European WiFi frequency). In addition, signs of health effects are now being reported from exposure to smart-meter frequencies (Maish, 2012).

A publication by Hallberg and Oberfeld (2006) noted an increasing incidence of EHS estimated from surveys carried out in various countries. According to the authors, if the growth found in the survey data continued linearly, then at least half the population could be suffering from EHS by 2017. Another study by Havas (2013) considered the most conservative estimate as 3% for severe EHS and 35% for light to moderate EHS, and applied this to the populations of Canada, USA, Europe, finding 25 million severe EHS sufferers, and 300 million light/moderate. These figures also hint at possible pandemics.

The WHO (2004) held an international workshop in Prague on EHS, which was defined as: 1) “a phenomenon where individuals experience adverse health effects while using or being in the vicinity of devices emanating electric, magnetic, or electromagnetic fields”; 2) “whatever its cause, EHS is a real and sometimes a debilitating problem for the

affected persons ... Their exposures are generally several orders of magnitude under the limits of internationally accepted standards". The hoped-for recognition of EHS by the WHO, in their next classification of diseases expected in 2015, would bring with it a rational and fundamental approach to diagnosis/treatment/prognosis, for the many people without response from the health systems of their individual countries, and marginalized by society. All fully respecting the unalienable right to health.

The pathogenesis of EHS is unclear, though increasing evidence points to a causal link between the pathological processes and development of the syndrome:

- in a recent, widely influential publication, Pall Martin (2013) underlined how EMFs (both high and low frequency) can have significant interaction at L-type voltage-dependent calcium-channel level, stimulating and so inducing significant increase in calcium-ion flow at intracellular level, which can lead to formation of peroxynitrite and free radicals, with consequent damage to cell structures. At the same time, calcium ions play a critical role in the release of neurotransmitters, generating the potentials of action and maintaining cell membrane integrity and nervous system function. Several studies show that alteration of calcium-ion homeostasis, e.g., resulting from EMF interaction at hippocampus level, can lead to neuron damage (memory loss, learning deficit) (Maskey et al., 2010; Fragopoulou et al., 2010b). The alteration of such cognitive functions can be seen in subjects exposed to EMF emitted by MPs, as widely confirmed (Preece et al., 1999; Koivisto, Krause, Revonsuo, Laine & Hamalainen, 2000). The findings of a meta-analysis on possible effects of MPs on brain bioelectric activity are worth noting: of 55 studies 37 show positive effects (Marino & Carrubba, 2009);
- a major role in EHS pathogenesis may be played by the hormone melatonin, involved in many physio-pathological processes – regulation of daily rhythms (including sleep/wake cycle), and modulation of the immune system – as powerful endogenous antioxidant. Some studies (Burch et al., 2002; Wood, Loughran & Stough, 2006) have shown that exposure to high/low frequency EMF brings about a significant reduction in melatonin serum level – determined partly through evaluation of its metabolites found in urine, 6-

hydroxymelatonininsulfate. This fall in circulating melatonin causes a number of humoral and hormonal changes, which in turn bring about various adverse effects such as sleep problems, as documented by Altpeter et al. (2006) in relation to an short-wave radio station in Switzerland;

- in one of their studies, Buchner and Eger (2011) observed a significant dysregulation of the catecholamines (adrenalin, noradrenalin, dopamine, phenylethylamine) in subjects exposed in the home environment to radiation from MP radio stations. These neurotransmitters are involved in the function of the autonomous nervous system, in response to stress and in alertness. Havas and Marrongelle (2013) found alterations in heart rate variability in controlled, repeated studies on volunteers, showing that EMF, in this case from a cordless phone base, at 2.4 GHz, impact the autonomous nervous system with significant up-regulation of the sympathetic nervous system;
- Hocking and Westermann (2003) explained that, for the genesis of dysaesthesiae at level of facial skin and scalp in MP users, nociceptive fibers (in particular C-fibers) may be involved.

As mentioned, in Sweden (Johansson, 2006), EHS is recognized as a functional impairment: EHS sufferers are thus eligible for support under the Swedish Act regarding Support and Services for Persons with Certain Functional Impairment. The Council of Europe (2011) has issued a report that requires open information about the locations of EMF sources, such as MP base stations and power lines, recognizing EHS sufferers and requiring that they have adequate protection. The report indicates 29 countermeasures, including “Calls on Member States to follow the example of Sweden and to recognize persons that suffer from electrohypersensitivity as being disabled so as grant them adequate protection as well as equal opportunities” (European Parliament, 2009). Moreover, the Council of Europe (2011) underlined the need to: “pay particular attention to ‘electrosensitive’ persons suffering from a syndrome of intolerance to electromagnetic fields and introduce special measures to protect them, including the creation of wave-free areas not covered by the wireless network”.

In the USA, the Architectural and Transportation Barriers Compliance Board has stated that EHS and multiple chemical sensitivity are to be considered disabilities under the Americans With Disabilities Act. Furthermore, the US National Institute of Building Sciences has recommended that spaces in commercial and public buildings be constructed with low EMF or chemical levels. The purpose is to ensure accessibility to any new build for EMF- and chemical-sensitivity sufferers (Indoor Environmental Quality, 2005). The Canadian Human Rights Commission reported that ~3% of Canadians have been diagnosed with environmental sensitivities (including both the above), and recommends environmental quality be improved in the workplace (Sears, 2007). The Austrian Medical Association (2012) provides a temporary code (Z58.4, exposure to radiation) under the 'International Classification of Disease, 10th Edition', to be used for EMF syndrome (their term for EHS).

USE OF MPs BY CHILDREN AND ADOLESCENTS

Electronic devices are being adopted by ever-younger users, and kept or held increasingly close to the body. These RF-emitting devices include MPs, tablets, and other wireless-technology instruments. Children and teenagers use them intensely, often round the clock. The incorrect and excessive use of these technologies stems from poor knowledge about their operation and possible health risks, and therefore lack of guidance (especially by parents) on necessary precautions. Youngsters are therefore being encouraged to use these devices, conceived as highly innovative and useful for staying in touch. For instance, few are aware that smartphones can emit radiation continuously, even in 'off-line' or 'flight' mode, and that emission power depends on network coverage: where this is poor, through congestion or remoteness of base station, the phone emission rises to secure communication.

Experience over a decade of seminars in Italian middle- and high-schools and interviews with students has enabled A.P.P.L.E. to build up a picture of how these devices are being used: youngsters are now the main users of mobile communications and Wi-Fi technology, with most children (>90%) of middle/high-school age having an MP or access to a tablet or computer. At school, pupils 12 and above keep their MPs in their jeans' front

pocket, 'always on', ready to connect to chat rooms and social networks or download data, even where use is prohibited by Italian school regulations. Wi-Fi networks are available in most schools, where routers again are 'always on'. Furthermore, Wi-Fi is present in most homes (routers 'on' 24 h/day), as well as in our cities, on trains, on the metro, etc. Around 30-60% of youngsters, in particular girls, sleep with the phone 'on', either under the pillow or on the bedside table. During the night they often send or receive texts (up to 400-500 texts/24 h) or calls, download music, surf the web and social networks, and also use apps and games in other leisure activities.

Tests on MP-dependency in youngsters performed by several authors confirm lack of impulse control, use of MPs to combat negative moods, MP-abuse manifest in number of daily calls, messages, 'missed' calls or 'beeps', and in time spent in MP activity (Choliz, 2010). Commonest reported disorders include tiredness, stress, headache, anxiety, difficulty in concentration, and sleep disturbances (Soderqvist, Carlberg, & Hardell, 2008). Total exposure time of the so-called Generation App to the high-frequency EMF range (often unknown) has risen significantly. Moreover, phone company advertisements often lure young people with unlimited rates, portrayal of the MP as a plaything, and enticing new applications. Essentially, youngsters (aged 12-18) show behavior very similar to that outlined by the 2012 report on people aged 18-30 in 13 countries by a worldwide leader in networking (Cisco, 2012). Overall, Cisco find a relationship between real addiction to smartphones and wireless technologies, to such an extent that young people are finding themselves unable to live without their devices, which they treat almost with affection. One outcome is that they are encountering problems in real 'face to face' relationships with their peers, preferring those mediated by their MPs.

But MP exposure brings other risks: many studies have found biological effects on health, as noted. In particular, children and young adults are still developing and consequently more sensitive to RF: a child's brain shows a SAR higher than an adult's (Gandhi, Lazzi, & Furse, 1996; Han, Gandhi, & de Salles, 2010; Gandhi et al., 2012). RF have negative influence on intellectual development and cognitive functions (Markov &

Grigoriev, 2010), including the development of epileptic syndrome (Grigoriev & Sidorenko, 2011). Adolescents adopting MPs have a malignant brain tumor risk five times that of non-users (Hardell, Carlberg, & Hansson-Mild, 2011b). Effects on fertility in young males, e.g., significant progressive decrease in sperm motility and increase in sperm DNA fragmentation, have demonstrably been linked to use of Wi-Fi computers held on the lap or MPs kept in front pockets (Avedano, Mata, Sanchez-Sarmiento, & Doncel, 2012). Prenatal exposure to MPs is found to be associated with behavioral difficulties in the child, e.g., hyperactivity around school age (Hocking, 2009; Divan, Kheifets, Carsten, & Olsen, 2010; Martine et al., 2010).

Medical groups and associations in Europe and the USA have published many recommendations on limiting use of MPs and wireless devices by children and adolescents (Grigoriev 2008; Grigoriev, Nikitina & Grigoriev, 2011; Environmental Health Trust, 2014), some of which have been taken up worldwide (Safer Phone Zone, 2011). The European Parliament (2009) noted the call for caution from Interphone coordinator Elisabeth Cardis, who recommended that children should not use MPs “beyond reasonable limits and that landlines should be preferred”. Concerning the protection of children, the Council of Europe (2011) stated that governments must “develop within different ministries (education, environment and health) targeted information campaigns aimed at teachers, parents and children to alert them to the specific risks of early, ill-considered and prolonged use of mobiles and other devices emitting microwaves” and “for children in general, and particularly in schools and classrooms, give preference to wired Internet connections, and strictly regulate the use of mobile phones by schoolchildren on school premises.” These resolutions were unheeded by the European Commission.

The Seletun Scientific Statement (Fragopoulou et al., 2010a) recommends lower limits for EMF and wireless exposures, based on reporting health effects for much lower exposure levels. Low intensity RF radiation can induce oxidative stress in cells, related to overproduction of reactive oxygen species damaging proteins, lipids, DNA, and resulting in diseases including cancer (Box 3). These non-thermal effects have been documented for

RF intensity of $0.1 \mu\text{W}/\text{cm}^2$, corresponding to $0.6 \text{ V}/\text{m}$ and SAR of $0.3 \mu\text{W}/\text{kg}$ (Yakimenko, Sidorik, Henshel, & Kyrylenko, 2014). Unfortunately, the safety limits (by international commissions) are based only on thermal effects and allow a SAR of $2 \text{ W}/\text{kg}$ for MPs. Johansson (2013) explains: “The body of evidence on electromagnetic fields requires a new approach to protection of public health; the growth and development of the fetus and of children and argues for strong preventative actions. These conclusions are built upon prior scientific and public health reports documenting the following: 1) low-intensity (non-thermal) bio-effects and adverse health effects are demonstrated at levels significantly below existing exposure standards; 2) ... public safety limits are inadequate and obsolete with respect to prolonged, low-intensity exposures; 3) new, biologically-based public exposure standards are urgently needed to protect public health world-wide; 4) it is not in the public interest to wait”.

FUTURE DIRECTIONS

Our examination of literature data, together with meta-analyses by ourselves and others, points to the conclusion that even today the risk of head tumors resulting from MP use is very high. A few years ago Lloyd-Morgan (2009) – though underestimating number of cell users by 50%, excluding cordless users, and assuming a minimum 30-year latency – calculated “there would be about 1900 cellphone-induced brain tumors out of about 50,000 brain tumors diagnosed in 2004, increasing to about 380,000 cell-phone-induced brain tumors within 2019 in the USA alone,” which would require “an increase in health costs of an annual US\$ 9.5 billion and the need for a 7-fold increase in number of neurosurgeons”. An estimate of head tumor incidence must begin with the correct number of cellphone users (6.8 billion subscriptions, 4.4 billion MP users worldwide by year’s end 2013), should include risk to cordless users, and assume at least a doubling of brain tumor and acoustic neuroma incidence as documented by Hardell already after ≥ 10 -15 year latency (Hardell, Carlberg & Hansson-Mild, 2006a,b; Hardell, Carlberg, Soderqvist & Hansson-Mild, 2013a,b).

A number of factors raise concern even further: 1) latency of MP-induced head tumors can exceed 30 years; 2) risk is higher in those starting MP use when young, with as yet <10 years accumulated latency; 3) the young are making ever-increasing use of MPs; 4) Hardell's data on increase in other types of malign and benign head tumor (besides brain gliomas, meningiomas, acoustic neuromas) remain chiefly indicative; 5) habitual and long-term MP use is possibly associated with increased risk of other head tumors, such as thyroid tumors (Feinmesser, 2013), ocular melanomas (Stang et al., 2001), tumors affecting epiphysis (Benson et al., 2013), salivary and parotid glands (Sadetzsky et al., 2008; Duan, Zhang & Bu, 2011).

Governments should promote educational campaigns targeting young people, parents, teachers and educators, in particular. This awareness-raising should aim at reducing exposure of young people, and be based on prudent public health planning principles rather than certainty of effect: 1) additional protection for children and fetuses, their being more vulnerable to health risks; their exposures are largely involuntary and they are less protected by existing public safety standards, despite comprising ~half the population; 2) recommended use of "land lines" or fiber optic cables; 3) encouraged use of unlimited landline rates at home, school, office, anywhere people are not "mobile"; 4) limitation of advertisements targeting children and adolescents, which in any case should clearly state possible health risks; 5) inclusion of SAR on MP packaging; 6) adoption by utility companies of SmartGrid-type projects that avoid new exposure to wireless components.

Governments should consider: what harm might result from failure to protect people, especially children, in terms of social costs alone, if the next few years see further confirmation that exposure to MPs can result in damage to health? Instead, what harm might result from adopting the Precautionary Principle, even if exposure to MPs should prove harmless?

We believe the situation being evaluated today represents just the tip of an iceberg: only time will tell the true dimensions. Even so, our analysis already reveals a clear

increase in tumor risk, and, even if partly proven, shows that MP use could undoubtedly lead to a dramatic health crisis. Today there is sufficient evidence to warrant application of the Precautionary Principle, aimed at substantial reduction in RF exposure limits: 1) risks from MP exposure should be publicized; 2) the spread of wireless technologies in schools should be limited; 3) MP use by minors should be discouraged; 4) prudent low-cost voluntary options should be encouraged (BioInitiative, 2012; EEA, 2008, 2013; European Parliament, 2009; Gee, 2009; Khurana, Teo, Kundi, Hardell & Carlberg, 2009; Kundi, 2009; Lloyd-Morgan, 2009; Radiation Research Org., 2009; Carpenter, 2010; Council of Europe, 2011; Gandhi et al., 2011). To this purpose, a 10-point list of simple personal actions designed to substantially reduce exposure to MP radiation was produced by a group of Viennese medical officers in 2006, and later adopted by the Ministère des Affaires Sociales et de la Santé (2012), A.P.P.L.E., as well as by several other groups such as BioInitiative (2012), and Environmental Health Trust (2014).

Should any doubt remain, it is worth outlining the consequences of the various scenarios with MP RF listed by Gee (2009): the first is similar to the cases where precautions were not taken and avoidable harm was not prevented; the second is where precautions avert much potential harm, whilst stimulating more sustainable innovation in the production and use of technologies; the third is where such precautions are taken but turn out to have been unnecessary. A fourth is that no precautions are taken and no convincing harm emerges.

We do not know which scenario will unfold, but we do know that a choice over current and future RF exposures must be made now, if the costs of possibly being wrong are to be minimized, in particular for our offspring. The tragedy is that the unfolding story of RF looks set to become another case of history repeating itself – following in the tracks of ionizing radiations, asbestos, tobacco smoke, and many other now demonstrated human carcinogens, where evidence of harm was officially recognized only a score or more years after the initial warnings.

Given the evidence we already have, this time we can act early, rather than giving cause for future generations once again to regret our inaction. The choice is ours: "To act or not to act" muses Gee (2009), echoing Hamlet's uncertainty. We call for government and protection agencies to unmask the dilemma: there is sufficient evidence, and the Precautionary Principle alone calls for action now.

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KEY TERMS

Electromagnetic fields, radiofrequencies, mobile phones, causation link, head tumors, electrohypersensitivity, conflicts of interest, business bias, awareness-raising, prudent avoidance.