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Effects of low-level radio-frequency (3 kHz to 300 GHz) energy on human cardiovascular, reproductive, immune, and other systems: A review of the recent literature $\stackrel{\sim}{\sim}$

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Abstract

Objectives: Occupational or residential exposures to radio-frequency energy (RFE), including microwaves, have been alleged to result in health problems. A review of recent epidemiological studies and studies of humans as subjects in laboratory investigations would be useful.

Methods: This paper is a narrative review of the recent medical and scientific literature (from mid-1998 through early 2006) dealing with possible effects of RFE on humans, relating to topics other than cancer, tumors, and central nervous system effects (areas covered in a previous review). Subject areas in this review include effects on cardiovascular, reproductive, and immune systems.

Results: A large number of studies were related to exposures from cellular telephones. Although both positive and negative findings were reported in some studies, in a majority of instances no significant health effects were found. Most studies had some methodological limitations. Although some cardiovascular effects due to RFE were reported in epidemiological studies (e.g., lower 24-h heart rate, blunted circadian rhythm of heart rate), there were no major effects on a large number of cardiovascular parameters in laboratory studies of volunteers during exposure to cell-phone RFE. In population-based studies of a wide range of RFE frequencies, findings were equivocal for effects on birth defects, fertility, neuroblastoma in offspring, and reproductive hormones. Some changes in immunoglobulin levels and in peripheral blood lymphocytes were reported in different studies of radar and radio/television-transmission workers. Due to variations in results and difficulties in comparing presumably exposed subjects with controls, however, it is difficult to propose a unifying hypothesis of immune-system effects. Although subjective symptoms may be produced in some sensitive individuals exposed to RFE, there were no straightforward differences in such symptoms between exposed and control subjects in most epidemiological and laboratory studies. Consistent, strong associations were not found for RFE exposure and adverse health effects. The majority of changes relating to each of the diseases or conditions were small and not significant.

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Conclusions: On the basis of previous reviews of older literature and the current review of recent literature, there is only weak evidence for a relationship between RFE and any endpoint studied (related to the topics above), thus providing at present no sufficient foundation for establishing RFE as a health hazard. Published by Elsevier GmbH.

Keywords: Radio-frequency energy; Radio-frequency radiation; Microwaves; Electromagnetic fields; Non-ionising radiation

Introduction

Background

In the six decades since the first report (Daily, 1943) of a lack of health hazards of low-level radio-frequency energy (RFE), a large number of publications have appeared in the medical and scientific literature relating to this topic. Although some European investigators may define RFE as being specifically limited to a frequency range of about 30 kHz to 300 MHz, the Institute of Electrical and Electronics Engineers Inc. uses the broader range of 3 kHz to 300 GHz to define the term. The latter (more inclusive) range will be used for purposes of this review (thus including the very-low frequency (VLF) range of 3-30 kHz, the ultra-highfrequency (UHF) range of 300 MHz to 3 GHz, the super-high-frequency range of 3-30 GHz, and the extremely high-frequency range of 30-300 GHz). Nowak and Radon (2004) noted that there are only a limited number of epidemiological studies in this area. There are also few studies of humans as subjects in laboratory investigations.

In a previous review, Jauchem (1998) addressed the 1995 to mid-1998 literature on all potential RFE-related human health effects. In another review, this author dealt with mid-1998 through 2003 literature limited to RFE effects on cancer, tumors, and the central nervous system (Jauchem, 2003). Since that time, other reviewers have included evaluation of cancer/tumors (Ahlbom et al., 2004; Kundi et al., 2004; Johansen, 2004; Leventhal et al., 2004; Moulder et al., 2005; Colonna, 2005) and effects on the central nervous system (Johansen, 2004; Leventhal et al., 2004). The authors of these previous reviews of the literature noted limited evidence for an association between RFE exposures and those health effects. Other than the topics mentioned above, the most-studied RFE research areas include the cardiovascular, reproductive, and immune systems. In the current paper, a summary is presented of original research studies (and subsequent commentaries with critical analyses of such studies) of RFE exposure in humans published from mid-1998 through early 2006. In addition, other less-studied topics, such as subjective symptoms and hematological changes are included. Other reviews of RFE exposure studies of humans are also summarized.

Since magnetic resonance imaging involves static and time-varying magnetic fields in addition to RFE, it may be difficult in some instances to determine effects due to each of these factors separately. For this reason, magnetic resonance imaging is not included in this review. In addition, specific effects of magnetic fields coincidentally associated with sources of RFE (such as e.g., mobile telephones) (Jokela et al., 2004) are not covered.

Articles dealing solely with (a) potential therapeutic uses of RFE, (b) effects of RFE on medical devices (such as cardiac pacemakers and telemetry systems), (c) exposure of human cells *in vitro*, (d) modeling of RFE deposition in humans, (e) revision of exposure standards, (f) application of the precautionary principle to RFE, (g) exposure to high levels of RFE causing thermal responses, and (h) RFE health effects research in progress, are beyond the scope of this review.

While hand-held "cellular telephones" are used with the transmitter close to the head, the use of "mobile telephones" (mostly in automobiles) does not result in the same levels of exposure to the head. Despite this distinction, many authors use the two terms interchangeably. In the current paper, the terms used by the original authors will be stated.

Identifying the literature

Publications were identified from the following electronic databases: The National Library of Medicine's PubMed[®] (including MEDLINE[®] (Medical Literature Analysis and Retrieval System Online)), BIOSIS[®], EMBASE[®], Toxicology Literature Online (TOXLINE[®] Special), DART[®]/ETIC (Developmental and Reproductive Toxicology/Environmental Teratology Information Center), AGRICOLA, INSPEC[®], JICST (Japanese Information Center for Science and Technology), PASCAL (Institut de l'Information Scientifique et Technique, Centre National de la Recherche Scientifique), CAB Abstracts[®], Chemical Engineering and Biotech Abstracts, Life Sciences Collection, SciSearch[®], National Technical Information Service, Applied Science and Technology Abstracts, Academic Search Premier, Master FILE Premier, PsychINFO/ Psychological Abstracts, Aerospace Database, and the Online Computer Library Center's FirstSearch® (including General Science Index, Applied Science and

Technology Index, Electronic Collections Online, and ArticleFirst[®]). Search terms included radio-frequency, microwave, radio waves, radar, cellular phone, mobile phone, and electromagnetic. Some publications referring to RFE were not found under these search terms, but rather were identified coincidentally. Since the use of electronic databases alone may not identify all relevant articles for a particular topic (Hopewell et al., 2002), "hand searching" of a number of journals was incorporated in the preparation of the current paper. Articles found from the sources listed above were examined in SciSearch[®] for additional references. Google Scholar[®] was searched for any additional references (Steinbrook, 2006).

In the current paper, the term "publication" generally refers to that defined by Easterbrook et al. (1991); therefore, book chapters, abstracts, and proceedings of meeting presentations were not included. Other items from the "gray literature" (Alberani et al., 1990), such as technical reports, official documents not published commercially, and pre-prints, were also not reviewed. Some of these items, however, were used when discussing the relevance of other reviewed articles. Letters-tothe-editor were discussed if they contained critical assessment of original studies and were published in peer-reviewed journals. "News" items (as identified by PubMed[®]), however, were generally not used for the review.

Information in English-language abstracts of non-English-language papers was included, but translations of the entire papers were not reviewed. When abstracts of non-English publications were not available, the papers were still cited. (Stroup et al. (2000) have recommended that any meta-analyses performed in the future on any topic should include non-English papers.)

Unlike many other reviews, there were no strict "inclusion criteria" (Weed, 1997) for papers listed. Basic assessment of acceptable study design and sample size, unbiased data collection, statistical methods, and adequate description of RFE exposure could be completed for most, but not all, studies. In contrast with a systematic meta-analysis, this narrative review is intended to provide the reader with a comprehensive summary of the existing literature, including both quantitative and qualitative findings.

Cardiovascular system (including cerebral blood flow)

Heart rate and blood pressure during occupational exposures

Gadzicka et al. (1997) evaluated a large number of parameters derived from 24-h blood pressure and heart

rate measurements from radio-station workers. A "day/ night heart rate variability indicator" was significantly lower, compared with a control group. This type of blunted circadian rhythm has been associated with adverse cardiovascular effects in some studies (e.g., Verdecchia et al., 1998).

In another study (Bortkiewicz et al., 1997), a higher percentage of workers at AM broadcast stations had more abnormalities in the electrocardiogram (ECG) (both resting and 24-h results combined) when compared with workers at radio-link stations (presumed to have low RFE exposure). Abnormalities in either resting ECG or 24-h ECG individually, however, were not significantly different between the two groups of workers. Szmigielski et al. (1998) reported no changes in mean values of mean, systolic, and diastolic blood pressures or in heart rates in workers presumably exposed to RFE, compared with controls. Day/night ratios and amplitudes of diurnal rhythms of heart rate and blood pressure, however, were significantly lower. The authors concluded that RFE "can evoke measurable cardiovascular effects, but, so far, no potential hazards can be assigned to these effects."

Wilén et al. (2004) found a significantly lower 24-h heart rate in operators of RFE plastic sealers versus control subjects. The authors noted, "due to the relatively few individuals in the study, it was not possible to adjust for confounding factors The impact of the healthy worker effect cannot be ne-glected." In another study, 35-min exposures to cellular phones (900 and 1800 MHz) with maximum allowed antenna powers had no significant effects on heart rate or blood pressure (Tahvanainen et al., 2004). An extensive set of test conditions included controlled breathing, spontaneous breathing, head-up tilt table test, Valsalva maneuvers, and deep breathing tests.

Vangelova et al. (2006) reported increases in blood pressure and blood levels of cholesterol in broadcastand television-station operators, compared with radiorelay station operators (presumed to have low RFE exposure). The authors, however, noted that working conditions such as "monotony and extended shifts" could have influenced the results. Atlasz et al. (2006) concluded that, on the basis of their study of heart rate variability, RFE from cell phones do not cause noticeable effects on heart rate regulation in healthy males and females.

Heart rate and blood pressure during experimental studies

Mann et al. (1998a) examined effects of pulsed 900-MHz fields on heart rate variability in humans during sleep. There were no significant effects of RFE on any of the relatively large number of parameters that were analyzed statistically (including, for three individual sleep stages: mean ECG R–R interval; total variability of R–R intervals; various spectral analyses of ECG very-low-frequency, low-frequency, and high-frequency bands; and normalized ECG frequency components related to the sum of power in specific bands (as standardized by Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Huber et al. (2003) observed slight decreases in heart rate of subjects exposed to RFE before sleep, but only during a limited number of sleep stages. There were no effects during RFE exposure while subjects were asleep.

In 40 subjects, Braune et al. (2002) measured blood pressure, heart rate, and cutaneous capillary perfusion during periods of cell-phone exposure, compared with placebo periods. Any changes were independent of cellphone exposure. Bortkiewicz et al. (2003) reported "a significant relationship between blood pressure and neurovegetative regulation disorders and exposure parameters" of mobile-phone RFE in occupationally exposed workers. The study seemed to be related to lifetime dose levels, but there were not enough details in the English-language abstract to allow further evaluation. In a study of 40 pregnant women, cell-phone RFE was not associated with baseline fetal heart rate or fetal heart rate acceleration/deceleration (Celik and Hascalik, 2004) during a "non-stress test" (per authors, "an ultrasound examination of a fetus that measures fetal well-being by correlating fetal movement with changes in fetal heartbeat").

Müller et al. (2004b) found no changes (compared with sham exposures) in heart rate, P–Q, Q–S and S–T ECG intervals, systolic and diastolic blood pressure, skin conductance, or skin temperature, or respiration, due to 77-GHz RFE exposure. In a follow-up study, the same investigators exposed subjects to a sequential pattern of RFE at frequencies varying from 5.8 to 110 GHz (Kantz et al., 2005). There were no significant effects of RFE on heart rate, systolic and diastolic blood pressure, skin conductance, or skin temperature. Because of the high frequencies applied, penetration depth would have been low, with possible subtle effects on skin conductance and temperature directly in the irradiated area, which was relatively small and difficult to measure.

In a study comparing numerous physiological parameters between subjects "experiencing subjective symptoms when using mobile phones" and control subjects (Wilén et al., 2006), only one measure of heart rate variability was different between the groups. Although the biological significance of this dissimilarity is unknown, the authors hypothesized that subjects reporting symptoms may exhibit "a shift in autonomic regulation towards sympathetic activity." Nonetheless, the difference between groups was not related to actual experimental RFE exposure.

Local blood flow changes

Khudnitskii et al. (1999) reported "significant changes in local temperature and in physiologic parameters of central nervous and cardiovascular systems" during cellphone exposure. No other details were listed in the English-language abstract. Paredi et al. (2001) found a significant increase in skin temperature of the ipsilateral nostril and occipital area during 30-min conversations on cell telephones. This was considered to be a local vasodilator response. Monfrecola et al. (2003) noted an increase in ear cutaneous blood flow due to cell-phone exposure. An experimental series with the phone placed against the ear, without power on, would have been useful for comparative purposes.

Huber et al. (2002) concluded that pulse-modulated 900-MHz RFE was associated with an increase in cerebral blood blood. Haarala et al. (2003) reported a somewhat increased (though not significantly) cerebral blood flow (measured by positron emmision tomography scanning) during digital cell-phone exposures. The authors surmised that the phenomenon resulted from an auditory signal produced by the phone battery. (This interpretation, however, was incorrect on the basis of results of a later study (Aalto et al., 2006) in which the problem was circumvented by using a remote power control.) Huber et al. (2005) found a statistically significant increase in cerebral blood flow, specifically in the prefrontal cortex, during exposure to "handsetlike" cell-phone RFE, but not to "base-station-like" RFE. They attributed the change to stronger lowfrequency components (below the RFE spectrum). Aalto et al. (2006) reported changes in regional cerebral blood flow due to mobile phone exposure. Blood flow was decreased in the posterior inferior temporal cortex (close to the position of the antenna), but increased in the superior and medial frontal gyri.

General cardiovascular disease and mortality

Tikhonova (2003) reported a high prevalence rate of cardiovascular disease in personnel working at a civil aircraft radar-tracking system. Details of exposure determination could not be discerned from the English abstract.

Breckenkamp et al. (2003) reviewed cohort studies of RFE occupational exposure and noted that, in all three studies pertaining to circulatory diseases, lower mortality rates were reported for exposed individuals. The most recent of these studies was by Groves et al. (2002). There were several shortcomings in this study; however, including insufficient exposure assessment (e.g., a substantial portion of those classified as "high-exposure" may not have been exposed at all). In another study, television station workers, presumed to be exposed to RFE (selected on the basis of length of service), also exhibited lower mortality rates associated with cardiovascular disease (Solenova et al., 2004). In contrast, Tikhonova et al. (2004) reported higher risks for hypertension and coronary artery disease in workers "running radiotechnic and communication equipment." Common problems in these types of studies are the healthy-worker effect and other effects due to socio-economic factors, medical support, and lifestyle.

Effects of natural RFE emission (solar radio flux)

Apart from man-made RFE, some investigators have suggested a link between intensity of radio-wave emission from the sun and adverse effects on the cardiovascular system. The intensity of RFE often increases during solar flares and the appearance of large sunspot groups. In addition, the sun produces a background radio flux, which varies in the course of the solar cycle. The maximum intensity of a solar RFE burst at a given frequency, e.g. at 606 MHz, may be only about 10^{-14} W/m² (Castelli and Guidice, 1972). Energy is emitted, however, over a wide range of frequencies. Since solar flares are associated with many factors other than RFE (e.g., protons and other particles, and disturbances in the geomagnetic field), articles indexed under the terms "solar activity" or "heliogeophysical," without some specific relationship to RFE (as measured by radio flux), are not covered in the current review.

Stoupel (1998) summarized some of his previous work, noting that "radio-wave propagation in the noon hours" was significantly correlated with myocardial infarction death rate. As mentioned previously by Jauchem (1997), however, the large number of geophysical parameters and categories of death analyzed without correction for multiple statistical comparisons make the results difficult to interpret. In other studies of a similar phenomenon (geomagnetic activity) and myocardial infarction mortality, after normalizing the data to remove weekly and seasonal variations, previously reported significant associations disappeared (Lipa et al., 1976).

Villoresi et al. (1998) reported a statistically significant increase in myocardial infarction associated with "days of the descending phase of cosmic ray Forbush decreases," a measure associated with solar radio-wave emissions (Gurnett and Kurth, 1995). Studies of this type (specifically on the cardiovascular system), however, must include consideration of possible confounding factors such as weather changes (Ebi et al., 2004).

Stoupel et al. (1999) reported relationships between deaths from stroke/ischemic heart disease and solar activity (including radio flux). Correlations, however, were negative for ischemic heart disease regarding subjects under age 65, but positive for subjects over age 74 (with no correlation for those between age 65 and 74). In another study (Stoupel et al., 2002), there was a negative correlation between ischemic heart disease and solar activity for subjects over age 74. In a study limited to oncology patients, the number of deaths (presumed due to cardiopulmonary arrest) was also inversely correlated with solar radio flux (Stoupel et al., 2003). With the different results between the studies, it is difficult to produce a unifying hypothesis of RFE effects. But in even the most recent study by Stoupel et al. (2004), numbers of deaths from cerebrovascular accidents and myocardial infarctions were inversely correlated with solar radio flux. This would argue against any detrimental health effects of natural RFE emissions.

A summary of original studies of RFE effects on the cardiovascular system is presented in Table 1, with this author's opinion of potential effects on health. In some cases, caveats to be considered when analyzing such effects, are included.

Reproductive system

Birth defects or fetal loss - original studies

In a case-control study, after controlling for potential confounders low birth weight was associated with presumed exposure among female physiotherapists to shortwaves (typically 27.12 MHz) (odds ratio 2.75; 95% confidence interval (CI) 1.07–7.04) (Lerman et al., 2001). In contrast, Cromie et al. (2002) found lower incidences of congenital malformations and miscarriage in physiotherapists than those in the general community. Physiotherapists, however, are part of a group of medical personnel that cannot easily be compared with the general population.

Mageroy et al. (2006) performed a cross-sectional study of personnel in the Royal Norwegian Navy. The authors concluded that service aboard a type of missile torpedo boat was associated with "an increased risk of having children with congenital birth defects and having children that were stillborn." The idea for the study was prompted by a previous report of emission of RFE used for electronic warfare on one particular ship of this type. Mageroy et al. (2006), however, concluded that the causes of their findings were unknown; no association with RFE was implied. Chia (2006) commented that even claiming an association with service aboard such a ship was premature, due to methodological issues that were raised by Mageroy et al. (2006) themselves. A combined effect of a multitude of factors, including RFE, cannot be ruled out.

Reference	Population	Reported effect
Heart rate (HR) and blood pro	essure	
Gadzicka et al. (1997)	Radio-station workers	\downarrow Day/night HR variability
Bortkiewicz et al. (1997)	Radio-station workers	Abnormal electrocardiogram
Szmigielski et al. (1998)	RFE workers	↓ Amplitude of diurnal HR and blood
2		pressure rhythms
Mann et al. (1998a)	Subjects during sleep	No cardiovascular effects
Braune et al. (2002)	Normal subjects	No cardiovascular effects
Bortkiewicz et al. (2003)	Mobile-phone users	"Neurovegetative regulation disorders"
Huber et al. (2003)	Normal population	Slight \downarrow HR before sleep
Celik and Hascalik (2004)	Pregnant women	No changes in fetal HR
Wilén et al. (2004)	RFE plastic sealer operators	↓ HR
Tahvanainen et al. (2004)	Normal subjects	No cardiovascular effects
Müller et al. (2004b)	Normal subjects	No cardiovascular effects
Kantz et al. (2005)	Normal subjects	No cardiovascular effects
Wilén et al. (2006)	Mobile-phone users who reported symptoms	No cardiovascular effects during RFE
when et al. (2000)	woone-phone users who reported symptoms	exposure
Vangelova et al. (2006)	Broadcast- and TV-station operators	↑ Blood pressure and cholesterol
Atlasz et al. (2006)	Healthy subjects	No changes in HR
× ,	meaning subjects	No changes in TIK
Local blood flow changes		
Khudnitskii et al. (1999)	Normal subjects	"Cardiovascular changes"
Paredi et al. (2001)	Normal subjects	Local vasodilator response
Monfrecola et al. (2003)	Normal subject	↑ Ear cutaneous blood flow
Huber et al. (2002)	Normal subjects	↑ Cerebral blood flow
Haarala et al. (2003)	Normal subjects	\downarrow Cerebral blood flow (but due to auditory
		signal, not RFE exposure)
Huber et al. (2005)	Normal subjects	Cerebral blood flow
Aalto et al. (2006)	Normal subjects	Both – and – in cerebral blood flow
General cardiovascular disease	and mortality	
Tikhonova (2003)	Radar system personnel	↑ Cardiovascular disease
Groves et al. (2002)	Occupational RFE exposure	Cardiovascular disease mortality
Solenova et al. (2004)	Occupational RFE exposure	↓ Cardiovascular disease mortality
Tikhovanova et al. (2004)	Occupational RFE exposure	↑ Coronary artery disease
Effects of natural PEE amissio	n (solar radio flux)	
Effects of natural RFE emission Stoupel (1998)	Myocardial infarction patients	↑ Myocardial infarction death rate
Villoresi et al. (1998)	General population	↑ Myocardial infarction death rate
Stoupel et al. (1998)	Persons with mortality due to stroke/	\downarrow Deaths if age <65, but deaths if age >75
Stouper et al. (1999)	ischemic heart disease	\downarrow Deaths if age < 03 , but deaths if age $> /3$
Stoupel et al. (2002)	Persons with mortality due to stroke/	\downarrow Deaths if age >75
Stouper et al. (2002)	ischemic heart disease	\downarrow Deaths II age > 13
Stoupel et al. (2003)	Oncology patients	↓ Deaths due to cardiopulmonary arrest
Stoupel et al. (2003) Stoupel et al. (2004)	Persons with mortality due to stroke/	· · · ·
Stouper et al. (2004)	ischemic heart disease	↓ Deaths
	ischemic neart disease	

Table 1.	Cardiovascula	r system
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Birth defects – reviews

Kirsner and Federman (1998) reviewed studies of video display units (VDUs) and noted that data relating to obstetric complications were inconsistent or methodically flawed. (Although VDUs are commonly considered as important regarding extremely low-frequency electromagnetic fields, they are included in the current review since they also emit RFE.) Robert (1999) reviewed epidemiological studies of intrauterine effects of electromagnetic fields; he suggested that no conclusion could be drawn for RFE due to a lack of data. Brent (1999) argued that potential effects of all types of radiation, including microwaves, "can be anxiety provoking to the public on two accounts, since reproductive failure engenders an unusual level of guilt and anger in the affected families, and radiation effects are misunderstood and feared by the public." He concluded that, in terms of biological plausibility, low-level electromagnetic fields (including RFE) have less of a potential to produce reproductive effects than other factors.

Regarding congenital malformations allegedly caused by RFE, Graham et al. (1999) maintained that too much emphasis is often placed on insufficient epidemiological data rather than on clinical findings that are readily available. Marcus et al. (2000) reviewed ten epidemiological studies of the association between VDU use and miscarriage. The authors concluded that work performed with VDUs in "modern offices" does not increase the risk for miscarriage.

Shi and Chia (2001) reviewed possible effects of occupational electromagnetic field exposure (including that from VDUs). The authors concluded that there was a lack of evidence for a strong association between maternal VDU- or microwave-oven exposure during pregnancy and adverse reproductive effects. Shaw (2001) agreed with previous reviews, indicating that evidence is lacking for a strong association between VDU use by women and fetal loss.

In a review that included epidemiological studies, Heynick and Merritt (2003) found no credible evidence of an association between chronic low-level RFE exposures of pregnant women or of fathers and anomalies in their offspring. Shields et al. (2003) reviewed both animal and human studies of short-wave diathermy and potential effects on pregnancy. No associations were reported for spontaneous abortion, premature births, stillbirth, or reduced fertility. Although congenital malformations and low birth weight were significantly associated with diathermy in some studies, several drawbacks were noted, including (a) lack of dose–response relationships, (b) potential of incidental findings, and (c) no association after multivariate analysis.

Feychting (2005) reviewed RFE effects on the developing child; the author noted "no specific type of malformation or other adverse outcome has been consistently reported."

Sex birth ratio

There were no original studies of RFE and sex birth ratio during the time period covered by this current review, but numerous papers were related to hypotheses of such effects. James (1997, 1998, 1999, 2001a) suggested that decreased male/female ratio in offspring due to RFE exposure was an indication of a reproductive hazard. Such a change in ratio was not strongly supported by RFE study data, but rather simply assumed to be true by James. Weyandt (1998) pointed out several problems with this concept of altered sex ratio. James (2001b, c, 2002) hypothesized that the supposed effects of RFE on sex birth ratio could be due to low testosterone/gonadotropin ratios in men. Safe (2001) responded that the concept of endocrine disruptors affecting human health was "intriguing and emotive," but that direct linkages between exposures to such factors with increased incidence of endocrine-related disease "are difficult to determine." Erdreich and Klauenberg (2001) noted that the majority of studies cited by James to support his contention of an altered sex ratio involved extremely low-frequency electromagnetic fields, not RFE. In a much earlier questionnaire study, Goerres and Gerbert (1976) had refuted "the argument that radar radiation in jet combat aircraft would, in some way, impair the procreation capability of the pilots"

Grajewski et al. (2002) agreed that more work on reproductive endpoints should be performed. The large number of environmental and other factors hypothesized to be associated with male/female offspring ratio, however, could make proof of an association with RFE somewhat challenging. These factors include biologic heterogeneity (Biggar et al., 1999), paternal age (Jacobsen et al., 1999; Jacobsen, 2001), maternal age (James, 2001d), season of child's birth (Nonaka et al., 1999), geographical latitude (Grech et al., 2000), pollution (Fertmann et al., 1997), exposure to metal fumes (Figá-Talamanca and Petrelli, 2000), exposure to polychlorinated biphenyls (del Rio Gomez et al., 2002), proximity to petrochemical, polymer, and chemical industrial plants (Mackenzie et al., 2005), and acute psychological stress (James, 1988, Zorn et al., 2002, Catalano et al., 2005). Hook (1981) also noted that the ratio could be influenced by many factors for which specific contributions may be difficult to determine, including socioeconomic status, race, and numerous demographic factors. In a more general sense, Davey-Smith and Ebrahim (2002) mentioned the poor control of confounding by standard statistical techniques, due to both (a) incomplete selection of potential confounders and (b) inevitable measurement errors in assessing the potential confounders that are included.

Decreased male/female sex birth ratio has reportedly been linked to testicular cancer (Jacobsen et al., 2000). In studies of RFE, however, there were no clear associations with testicular cancer (Jauchem, 2003).

Fertility

Hjollund et al. (1997) reported no significant differences in semen volume, sperm density and morphology, or immotile spermatozoa in Danish military personnel operating RFE systems, compared with other occupational groups. Schrader et al. (1998) found no significant differences in semen volume and sperm concentration, morphology, motility, or viability in military personnel with potential RFE exposures, compared with a control group. Irgens et al. (1999) analyzed semen in men undergoing infertility investigation who were exposed to various occupational factors. There was no significant change in semen quality in men presumably exposed to short-wave RFE.

Jung and Schill (2000) noted that electromagnetic fields (including RFE) could impair spermatogenesis by heat induction in the testicles, but only with excessive exposure. Decreased spermatogenesis may, in some cases, be considered less serious than abnormal quality of sperm (including morphology and motility) (Pohl et al., 2005). Grajewski et al. (2000) studied 37 different parameters in 12 male RF-dielectric-heater operators. When compared with 34 "unexposed" men, there were minor semen quality differences in exposed operators. These authors suggested that further studies were warranted.

It is important to realize that semen parameters have been shown to differ greatly between responders and non-responders to recruitment in epidemiological studies, and that investigators should expect non-representative samples in such studies (Cohn et al., 2002; Stewart et al., 2001). Selection bias, associated with sociodemographic characteristics, is common in studies of semen analysis (Muller et al., 2004a). In addition, Alvarez et al. (2003) noted that standard reference values for semen characteristics are of limited value due to marked variations between individuals. Despite these limitations, Liu et al. (2003) reported reductions in sperm motility and viability in radar operators, compared with a "lowly exposed group and control group." Details of such groups were not available. One factor not related to RFE ("abstinence time") was identified as "a dangerous factor" in terms of sperm chromatin structure assay.

Velez de la Calle et al. (2001) performed a populationbased case-control study of occupational and environmental exposures in military population. The only factors associated with infertility were (a) having worked as a submariner in nuclear-powered submarines and (b) having worked in very hot conditions. There was no significant association with exposure to RFE. Ding et al. (2004) noted an increase in "sperm dysmorphia" in subjects who worked with radar. The quality of semen "changed when radar electromagnetic wave frequency, distance, intensity, lasting time and protection shield were changing."

Fejes et al. (2005) reported that cell-phone use was negatively correlated with the proportion of rapid progressive motile sperm. In another study, however, of men "with a history of exposure to computers," there were no significant differences in sperm density, sperm viability, percentage of normally formed sperm, percentage of progressive sperm, and semen volume (Sun et al., 2005).

Kilgallon and Simmons (2005) found that "men who carried their mobile phone in their hip pocket or on their belt had lower sperm motility than men who did not carry a mobile phone or who carried their mobile phone elsewhere on the body." Few studies have been completed regarding demographic, social, and economic characteristics of cell- phone users and non-users. There are potential confounders that may affect an association between mobile phone use and semen quality.

Factors that may affect male fertility have been reviewed by Sheiner et al. (2003). In addition to RFE, these include solvents, heavy metals, and ionizing radiation. Derias et al. (2006) noted that studies of mobile-phone RFE and male fertility are "quite limited." Sallmén et al. (2005) have suggested that either time to pregnancy (the number of menstrual cycles required to conceive) or infertility rates may be better direct measures of fertility, rather than semen quality.

Andersen et al. (2000) found relatively low sperm counts during medical exams prior to military service. Vlassov (2000) facetiously pointed out that laptop computers have not been tested for their effects on the testes, even though RFE is emitted close to the testes. The author's point was to disparage the need for such research.

Neuroblastoma in offspring

De Roos et al. (2001) interviewed mothers and fathers in a case-control study of neuroblastoma in offspring (study population described by Olshan et al. (1999)). Parents were asked if they "worked within 30 ft of" any electrical equipment or RFE sources. An industrial hygienist then reviewed exposure information and, with a health physicist, classified persons as exposed or unexposed. A broad grouping of RFE sources was associated with insignificantly increased incidences of neuroblastoma for both maternal (odds ratio 2.8; 95% CI 0.9–8.7) and paternal (odds ratio 1.3; 95% CI 0.8–2.2) exposures. Overall, however, relatively low odds ratios of other groupings did not support a strong association between parental RFE exposure and neuroblastoma in offspring.

Reproductive endocrinology

De Seze et al. (1998a) studied subjects exposed to 900 MHz RFE emitted by a cell phone 2 h/day, 5 days/ week, for 1 month. There were no changes in serum luteinizing hormone and follicle stimulating hormone concentrations, at multiple sampling times. There was a trend toward reduced levels of prolactin during exposure.

In a study by Daşdağ et al. (1999), technicians at radio-broadcasting, radio-link, or television-transmitter stations exhibited higher blood levels of estradiol,

Table 2.	Reproductive	system
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Reference	Population	Reported effect
Birth defects		
Lerman et al. (2001)	Female physiotherapists	Low birth weight (no effects on spontaneous abortions, congenital malformations, or prematurity)
Cromie et al. (2002)	Female physiotherapists	↓ Congenital malformations, ↓ Miscarriage rate
Mageroy et al. (2006)	Navy personnel	No association with RFE
Fertility		
Hjollund et al. (1997)	Military personnel operating RFE systems	No effects on semen volume, sperm density, morphology, or motility
Schrader et al. (1998)	Military personnel operating RFE systems	No effects on semen volume, sperm density, morphology, motility, or viability
Irgens et al. (1999)	Men undergoing investigation for infertility	Improved semen quality
Grajewski et al. (2000)	RF-dielectric-heater operators	Minor effects on semen quality
Liu et al. (2003)	Radar operators	↓ Sperm motility and viability
Velez de la Calle et al. (2001)	Military members	↑ Fertility
Ding et al. (2004)	Radar workers	Sperm dysmorphia
Fejes et al. (2005)	Cell-phone users	↑ Proportion of rapid progressive motile sperm
Sun et al. (2005)	Computer users	No effects on sperm density, viability, percentage of normally formed sperm or progressive sperm, and semen volume
Kilgallon and Simmons (2005)	Mobile-phone users	↑ Sperm motility
<i>Neuroblastoma in offspring</i> De Roos et al. (2001)	Parents exposed to electrical equipment or RFE sources	↑ Neuroblastoma for some RFE exposure groups
<i>Reproductive endocrinology</i> De Seze et al. (1998a)	Cell-phone users	No changes in serum prolactin, luteinizing
		hormone, and follicle stimulating hormone concentrations
Daşdağ et al. (1999)	Radio and television technicians	↑ Blood estradiol, progesterone, and testosterone
Grajewski et al. (2000)	RFE-dielectric-heater operators	Slight - in follicle-stimulating hormone

progesterone, and testosterone. Control subjects were presumed to be occupationally unexposed to RFE. Some of the RFE-exposed technicians climbed television towers as part of their duties. Exertion could result in increased blood levels of estradiol and testosterone (Copeland et al., 2002). Grajewski et al. (2000) reported minor hormonal differences in RFE-dielectric-heater operators (compared with controls), including a slightly higher mean follicle-stimulating hormone level (7.6 versus 5.8 mIU/ml). Hocking and Andrews (2003) presented a case report

of a "radio officer" with "isolated hypogonadotrophic hypogonadism." Bortkiewicz (2001) reviewed human studies of RFE from cell phones and noted no changes in secretion of follicle-stimulating hormone or prolactin.

A summary of original studies of RFE effects on the reproductive system is presented in Table 2, with this author's opinion of potential effects on health.

Immune system

Radar, radio and television transmitters

Dmoch and Moszczynski (1998) reported an increase in immunoglobulin (Ig) G and IgA concentrations, increased lymphocytes, and lower T-helper/T-suppressor ratios in "workers of television re-transmission and satellite communication centers." Details of any control groups were not mentioned in the available Englishlanguage abstract. These changes were considered to have no clinical implications. In a follow-on study, Moszczynski et al. (1999) noted that, in contrast to the workers listed above, radar operators exhibited elevated IgM and decreased total T8 lymphocytes. This was assumed to "indicate that the effect of microwave radiation on the immune system depends on the character of an exposure." Again, the changes were not considered to have any clinical implications. Yuan et al. (2004) reported increased levels of IgM and Ig G, but no change in IgA, in subjects presumably exposed to low-intensity 170-MHz RFE.

Tuschl et al. (1999) indicated that exposures of medical personnel operating RFE units exceeded recommended exposure limits. There were no significant differences, however, between small groups of control and exposed persons in (1) total leukocyte counts, (2) total lymphocyte counts, (3) leukocyte subpopulations (determined by flow cytometry and monoclonal antibodies against surface antigens), and (4) lymphocyte proliferation after stimulation by phytohemagglutinin. All immune parameters were within normal ranges.

Tuschl et al. (2000) reported significantly higher numbers of natural killer cells (subset of lymphocytes) in workers using induction heaters (most of which included frequencies in the very low-frequency (VLF) range of 3–30 kHz), compared with controls. At least 18 different immunological parameters were measured and compared in this study. A decrease in monocyte phagocytic activity in these workers was counteracted by an increase in the number of active cells, indicating normal non-specific immunity. Thus, no substantial overall suppressive effect of RFE was found.

Garaj-Vrhovac (1999) compared peripheral blood lymphocytes drawn from 12 subjects "employed on radar equipment and antenna system service" with those from control subjects of a similar age. An increase in frequency of micronuclei was found in RFE-exposed subjects. The author stated that the results "showed an increase in ... disturbances in the distribution of cells over the first, second and third mitotic division in exposed subjects compared to controls."

Del Signore et al. (2000) studied parameters of immune function in (a) women living in one geographic area containing a relatively high number of radio/ television transmitters, compared with (b) female "white-collar staff and doctors" at a university in an adjacent geographic area. Women in group "a" above exhibited lower levels of interferon- γ produced by peripheral blood mononuclear cells than women in group "b". A sub-group (who had a predisposition to suffer from allergic diseases) of women in group "a" exhibited higher serum IgE levels. It would be difficult, however, to confirm that the groups were similar in all aspects apart from RFE exposure, including residential and occupational factors. In a parallel study by the same group (Boscolo et al., 2001), several measures of immune function were different between presumably RFE-exposed vs presumably non-exposed women. Serum IgE levels, however, were not different between groups. It is possible that some subjects were enrolled in both studies.

Cellular or mobile phones

Dabrowski et al. (2001) suggested there was a need for multidisciplinary studies, "comprising the wide spectrum of immune homeostatic tasks, including defensive, immunoregulatory and pro-regenerative capabilities of immune system exposed to rapid environmental spread of different electromagnetic emitters." Radon et al. (2001) found no effect of cell-phone exposure on salivary immunoglobulin A levels. The study, however, included only eight subjects. Because of the cross-over design, it wold have been preferable to show results stratified for sequence of exposure. Galeev (2000) proposed that "even prolonged and frequent use" of cell phones would probably be safe, since the immune system could adapt quickly. He suggested that exposure might even act to increase the resistance to stress in humans.

Kimata (2002, 2005) reported enhanced skin wheal responses and allergen-specific IgE production due to cell-phone RFE exposure in patients with atopic eczema/dermatitis syndrome, but not in normal subjects. In another study (Kimata, 2003), enhanced allergic responses in patients exposed to "frequently ringing mobile phones" were attributed to psychological stress. Such responses were reduced by "viewing a comic video" (Kimata, 2004). Since a double-blind cross-over trial was used (Kimata, 2005), however, ringing of the phones cannot account for the observed response.

A summary of original studies of RFE effects on the immune system is presented in Table 3, with this author's opinion of potential effects on health.

Subjective symptoms

Epidemiological surveys - cell/mobile phones

Oftedal et al. (2000) found that 13–31% of respondents in Norway and Sweden noticed at least one symptom (headaches, fatigue, sensations of warmth on or around the ear, or burning sensations in facial skin) in association with cell-phone use. The authors concluded that the results "suggest an awareness of the symptoms, but not necessarily a serious health problem." Szmigielski and Sobiczewska (2000) stated that the "development of non-specific health symptoms is possible, at least in 'RFE-sensitive' subjects." Clear evidence of a causal relationship between RFE and such symptoms, however, is lacking.

Sandström et al. (2001) hypothesized that users of cell-phone systems with pulse-modulated fields (i.e., digital phone systems) would experience more subjective symptoms than users of the analog phone systems. Upon investigation, however, no such increased risk was

Reference	Population	Reported effect
Radar, radio, and television tra	insmitters	
Dmoch and Moszczynski (1998)	Television center workers	↑ Immunoglobulin (Ig) G and A
Moszczynski et al. (1999)	Radar operators	↑ Ig M, — T8 lymphocytes
Yuan et al. (2004)	Subjects presumably exposed to RFE	\uparrow Ig G and M
Tuschl et al. (1999)	Medical personnel operating RFE units	No effect on leukocytes
Tuschl et al. (2000)	Workers using induction heaters	↑ Natural killer cells
Garaj-Vrhovac (1999)	Radar equipment workers	↑ Micronuclei in peripheral blood lymphocytes
Del Signore et al. (2000)	Women living in one area with many radio/ television transmitters	\downarrow Mononuclear-cell interferon- γ
Boscolo et al. (2001)	RFE-exposed women	Changes in several measures
Cell/mobile phones		
Radon et al. (2001)	Normal subjects	No effect on salivary Ig A
Kimata (2002, 2005)	Atopic eczema dermatitis patients	↑ Allergen-specific IgE production (but not due to RFE)

Table 3. Immune system

found. In fact, a statistically significant lower risk for sensations of warmth on the ear was found for digitalphone users compared with analog-phone users. The authors stated that, apart from factors related to RFE, digital and analog cell phones differ in size, shape, and audio quality. They surmised that audio quality disturbances could cause stress and indirectly result in neurasthenic symptoms. After a follow-up study using 2402 subjects from the previous investigation, Wilén et al. (2003) hypothesized that specific absorption rates, in combination with longer calling time per day, could be correlated with subjective symptoms.

Stenberg et al. (2002) noticed that many patients with perceived hypersensitivity to electricity reported aggravation of symptoms (which included headache) from cell-phone use. On the basis of a questionnaire survey, Bortkiewicz et al. (2004) noted that people living in the vicinity of cell-phone base stations reported "various complaints mostly of the circulatory system, but also of sleep disturbances, irritability, depression, blurred vision, concentration difficulties, nausea, lack of appetite, headache and vertigo." From another questionnaire, Al-Khlaiwi and Meo (2004) concluded "the use of mobile phones is a risk factor for health hazards" The data, however, were simply presented in a descriptive fashion. The authors listed numbers of headaches, fatigue, dizziness, tension, and sleep disturbance associated with "exposure durations" of <1, 1-5, and 5-10 years, but did not list numbers of subjects in each exposure category. The conclusion seemed to be based on a higher percentage of headaches reported by subjects with phone call durations of 60-120 min (versus subjects with durations of 5-10, 10-30, or 30-60 min). There was no control group of non-users. The actual pattern of mobile-phone calls may not be accurately represented by reports of users. Thus, the estimation of exposures by the use of questionnaire data is problematic (Parslow et al., 2003).

Balikci et al. (2005) noted "no effect on dizziness, shaking in hands, speaking falteringly and neuropsychological discomfort, but some statistical evidences are found that mobile phone may cause headache, extreme irritation, increase in the carelessness, forgetfulness, decrease of the reflex and clicking sound in the ears." The degree of control for selection bias and appropriateness of statistical analyses are unknown.

Szyjkowska et al. (2005) found that the most common symptom reported by mobile-phone users was a thermal sensation behind or around the ear and in the auricle. On the basis of a survey, Balik et al. (2005) suggested that mobile phone use was associated with "blurring of vision, secretion of the eyes, inflammation in the eyes and lacrimation of the eyes." Subjects participating in the survey reported "an awareness of the symptoms and sensations." In response to a questionnaire administered by Schüz et al. (2006), sources of extremely lowfrequency electric and magnetic fields were mentioned more often than RFE by subjects who attributed health complaints to non-ionizing radiation.

Seitz et al. (2005) reviewed a number of studies of subjects exposed to RFE associated with mobile phone communication. The authors reported no support for perception of RFE or for symptoms presumed to be related to "electromagnetic hypersensitivity."

Epidemiological surveys – occupational

Tachibana et al. (1998) suggested that the use of VDUs in the workplace was "associated with insomnia."

Nakazawa et al. (2002) used self-administered questionnaires to study seventeen subjective symptoms in users of VDUs. "Mental and sleep-related symptom scores" were found to be higher in workers using VDUs for more than 5 h/day than in groups with use of greater than one or between 1–3 and 3–5 h/day. Although some potential confounders were adjusted for, others (such as ergonomic workload and job stress) were not considered.

Wilén et al. (2004) reported no significant difference in the prevalence of subjective symptoms between RFE operators and controls. In a subsequent study, Wilén et al. (2006) (mentioned in section "Heart rate and blood pressure" above) also found no association between RFE exposure and symptoms.

Headaches

Frey (1998) suggested that reports of headaches in cellphone users "may be the canary in the coal mine, warning of biologically significant effects." Chia et al. (2000a, 2000b) reported an adjusted prevalence rate ratio of 1.31 (95% CI 1.00-1.70) for headaches in cell-phone users compared with non-cell-phone users. Hocking (2001a) complained that the investigators used a definition of headache that "would lead to imprecision in case ascertainment and hence a minimal estimate of the risk." Chia et al. (2001) responded that they used the International Headache Society Classification since it is in common use. In addition to headache, specific central nervous system symptoms were included in their study. It is apparent that the use of a cell phone could result in neck muscle strain, which could in turn result in fatigue or headaches.

Santini et al. (2002a) found no significant differences in headaches reported by cell-phone users compared with subjects not using cell phones. Only 7% of respondents to a questionnaire (Szyjkowska et al., 2005) related headaches to mobile-phone use. In another study, subjects living near mobile phone base stations reported more symptoms of headaches, fatigue, and concentration difficulty (Hutter et al., 2006). Although accuracy on cognitive tests decreased with increased RFE exposure levels, perceptual speed increased. Coggon (2006) suggested that some associations could have been chance occurrences due to the large number of different types of outcomes measured. That author also noted that similar symptoms have been reported due to other types of exposure (e.g., a wide assortment of different chemicals) without discernible causal mechanisms. In a study by Rubin et al. (2006), persons with self-reported sensitivity to mobile phone signals did not react to such exposures with any increased severity of headache symptoms.

Other studies relating to RFE and headaches are listed under the topic "Atmospheric RFE" below.

Laboratory experimental studies

Lebedeva and Kotrovskaya (2001) exposed 49 subjects to "electromagnetic field of extremely high frequencies" and examined whether or not the field could be sensed. The study was designed to investigate the association between sensing of RFE and EEG parameters, flicker fusion and other central and peripheral nervous system functions. Subjects were classified into three categories: (1) good perception with few false alarms, (2) poor perception with few false alarms, and (3) high perception with many false alarms. Numbers of subjects in each category were not given, making the results difficult to interpret.

Hietanen et al. (2002) studied 20 volunteers who considered themselves to be sensitive to cell phones. The number of reported symptoms was higher during sham exposure than during RFE exposure. None of the subjects could distinguish real RFE exposure from sham exposure. Although it is unlikely that sensing of cell-phone RFE is possible, symptoms may be produced in sensitive subjects. Such symptoms could become conditioned responses to the perception of a cell phone. The occurrence of symptoms under sham-exposure conditions does not rule out a contribution of RFE in the possible evolution of such hypersensitivity. Sham exposure was always the first or second exposure condition. On the basis of measurements of heart rate and blood pressure, the subjects may have become more relaxed during the course of subsequent experiments. The higher frequency of symptoms during sham exposure could have been due to higher postural load at the beginning of the experiment when subjects were not yet adapted to the experimental conditions.

Koivisto et al. (2001) reported no effects of cell-phone exposure on the subjective symptoms of headache, dizziness, fatigue, itching or tingling of the skin, redness on the skin, and sensations of warmth on the skin. (The experiments were designed to investigate cognitive effects of cell-phone exposure.) Except for a small increase in dizziness and fatigue (attributable to 1-h cognitive performance), most subjects experienced no symptoms at all. It is unfortunate that subjects were not followed up for several hours, since previous surveys have included symptoms being reported after a longer period of time.

Blackmore and Rose (2002) studied effects of a "bioelectric shield" device on mood changes during cell-phone exposure. The investigators concluded that a measurable placebo effect was produced. In a study by Straume et al. (2005), significant increases in temperature of the ear were due to thermal insulation by the phone and to heating of the phone from dissipation of electrical power, but not to RFE exposure itself.

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Case reports

Anecdotal reports of headaches, skin numbing, and memory loss due to cell-phone use have been mentioned without specific reports cited. For example, Cox and Luxon (2000) referred to cases they had collected of "disturbing symptoms" relating to the use of cellphones, including "dizziness, disorientation, nausea, headache, and transient confusion", but the authors acknowledged these cases were unpublished.

One cell-phone user was found to have permanent unilateral dysesthesia of the scalp, slight loss of sensation, and "abnormalities on current perception threshold testing of cervical and trigeminal nerves" (Hocking and Westerman, 2000). "Headaches, unilateral blurred vision and pupil constriction, unilateral altered sensation on the forehead, and abnormalities of current perception thresholds on testing the left trigeminal ophthalmic nerve" were reported in a male cellphone installation "rigger" (Hocking and Westerman, 2001). Westermark and Wisten (2001) presented a case report of a man who had sustained a zygomatic fracture and surgical treatment, including implantation of a miniplate. Subsequently, dysesthesia was associated with the use of a cell phone and with proximity to landing aircraft. It was thought that a surface current was created on the miniplate. Another case of dysesthesia in a cell-phone user was also reported by Hocking and Westerman (2002).

General discussion

Orbach-Arbouys et al. (1999) reviewed RFE and extremely low-frequency electromagnetic fields. The authors stated "electromagnetic radiation may play a role in a number of disorders such as depression and memory loss." Subjective symptoms reported in relation to cell-phone use include headache, feelings of discomfort, burning sensations in the facial skin, and warmth on or near the ear.

The terms "radio-frequency disease" and "radiofrequency sickness", though obsolete, have been mentioned recently in relation to cell-phone use (Santini, 1999, Santini et al., 2000) and RFE overexposures (Hocking and Westerman, 1999, Hocking, 2001b, c, Navarro et al., 2003). McRee (1972) previously stressed the limitations and inadequacy of work supposedly showing such a syndrome. He noted that in most studies, details such as the number of workers, the frequency, power level, type of radiation, and duration of exposure were not known or statistical findings were not reported. Rayman (1995) recognized that, although "radio-wave sickness" had often been described in Eastern Europe, it had never been demonstrated elsewhere. Other aspects concerning the inappropriateness of these terms have been discussed previously (Jauchem, 1997, 1998).

The topic of "electric hypersensitivity" (to frequencies lower than RFE) is beyond the scope of the current paper. Gobba (2002) observed there are no universally accepted diagnostic criteria or procedures for diagnosis of hypersensitivity to electromagnetic fields, including RFE.

A summary of original studies of RFE effects on subjective symptoms is presented in Table 4, with this author's opinion of potential effects on health. Simple case reports are not included.

Other effects

Hormones

De Seze et al. (1998a) (mentioned in section "Reproductive endocrinology" above) studied subjects exposed to 900 MHz RFE emitted by a cell-phone 2 h/ day, 5 days/week, for 1 month. There were no changes in serum adrenocorticotropin and growth hormone concentrations, at multiple sampling times. Thyrotropin concentration decreased during exposure weeks, and increased to baseline levels thereafter. Due to lack of details about statistical analyses, effects on this and other hormones cannot immediately be interpreted on the basis of the article alone. The authors, however, reported individual levels of thyrotropin. Using these data and appropriate statistical methods could reveal a significant effect of exposure.

In a study by Dasdağ et al. (1999) (mentioned in section "Reproductive endocrinology" above), technicians at radio-broadcasting, radio-link, or televisiontransmitter stations exhibited higher blood levels of triiodothyronine, tetraiodothyronine, and thyroid stimulating hormone. Control subjects were presumed to be occupationally unexposed to RFE. Some of the RFEexposed technicians climbed television towers as part of their duties. Exertion could result in increased blood levels of triiodothyronine and tetraiodothyronine (Hackney and Gulledge, 1994), and thyroid stimulating hormone (Bosco et al., 1996). Bergamaschi et al. (2004) administered a questionnaire to employees in various occupations who used cell phones. There was a greater prevalence of subjects with low levels of thyroid stimulating hormone among workers with conversation times of more than 33 h/month, compared with shorter times. The authors noted that the results could have been due simply to the stress associated with using cell phones, rather than exposure to RFE.

In a study by Vangelova et al. (2002), changes in the circadian rhythm of 11-oxycorticosteroids and increased variability of catecholamine secretion were seen in satellite-station operators (presumably exposed to

Reference	Population	Reported effect
Epidemiological surveys – cell/r	nobile phones	
Oftedal et al. (2000)	Respondents to a survey	Awareness of symptoms
Cox and Luxon (2000)	Cell-phone users	"Disturbing symptoms"
Sandström et al. (2001)	Mobile-phone users	↓ Sensation of warmth on ear for digital vs. analog users
Stenberg et al. (2002)	Patients with perceived hypersensitivity to electricity	Reports of symptom aggravation
Wilén et al. (2003)	Mobile-phone users	↑ Sensation of warmth on ear with higher absorption rates
Wilén et al. (2004)	RFE operators	No change in symptoms
Al-Khlaiwi and Meo (2004)	Mobile-phone users	↓ Risk factor for health hazards"
Bortkiewicz et al. (2004)	Residents in vicinity of cell-phone base stations	"Various complaints"
Szyjkowska et al. (2005)	Mobile-phone users	↑ Thermal sensation around ear
Balik et al. (2005)	Mobile-phone users	Awareness of uncomfortable eye symptoms
Wilén et al. (2006)	RFE operators	No change in symptoms
Schüz et al. (2006)	Questionnaire respondents who attributed complaints to non-ionizing radiation	Sources of extremely-low-frequency electric and magnetic fields mentioned more often than RFE
Epidemiological surveys – video		
Tachibana et al. (1998)	VDU users in workplace	Insomnia
Nakazawa et al. (2002)	VDU users	↑ "Mental and sleep related symptom scores
Headaches		
Chia et al. (2000a, b)	Cell-phone users	↑ Headaches
Santini et al. (2002a)	Cell-phone users	None
Szyjkowska et al. (2005)	Questionnaire respondents	7% Headaches related to mobile-phone use
Hutter et al. (2006)	Subjects living near mobile phone base	↑ Headaches; ↑ perceptual speed on
	stations	cognitive tests
Rubin et al. (2006)	Subjects "sensitive" to mobile phone signals	None
Laboratory experiments		
Lebedeva and Kotrovskaya (2001)	Normal subjects	Unknown
Koivisto et al. (2001)	Normal subjects	None
Hietanen et al. (2002)	Subjects "sensitive to cell phones"	↓ In reported symptoms
Blackmore and Rose (2002)	Normal subjects	No RFE effects (placebo effect only)
Straume et al. (2005)	Normal subjects	None

Table 4. Subjective symptoms

low-level RFE). The authors suggested that clarification is needed regarding any possible health hazards associated with these observations. Vangelova and Deyanov (2003) reviewed this topic. In another study by Vangelova and Israel (2005), 12 broadcasting station operators with "high-level" RFE exposure were reported to have significantly increased excretion rates of cortisol, epinephrine, and norepinephrine. A control group consisted of 12 satellite station operators that were classified as having "low-level exposure."

Bortkiewicz (2001) reviewed human studies of RFE from cell phones and noted no changes in secretion of melatonin, growth hormone, or adrenocorticotropic hormone. Another study showed no effect of such RFE on melatonin in healthy subjects (Bortkiewicz et al., 2002). Braune et al. (2002) (study mentioned above, under "Cardiovascular system") found no changes in serum levels of norepinephrine, epinephrine, cortisol, or endothelin during periods of cell-phone exposure, compared with placebo periods. Jarupat et al. (2003) found significantly lower salivary melatonin in women during use of a cell telephone (30 min every hour, for 6 h), compared with sham exposures. An inhibition (due to local heating from the cell phone) of the normal decrease in brain temperature, during the evening hours, was postulated to be responsible for reduced melatonin secretion. An interaction with the pineal gland, however, cannot be discounted. Inhibition of nocturnal melatonin secretion due to physical activity (that interacts with core temperature decrease during the night) (van Someren, 2000) is much less pronounced than the effect observed in this study.

Although Mann et al. (1998b) found a significant increase in plasma cortisol in men exposed for 8 h to 900 MHz RFE pulsed at 217 Hz, the authors noted that the increase was only slight and transient. De Seze et al. (1999) reported no disruption of the circadian profile of melatonin in 37 male subjects exposed to RFE from two types of cell phones. Exposure, however, was during the evening hours, almost entirely during the phase of melatonin suppression. A shift in melatonin onset may have been the only change expected. Radon et al. (2001) found no effect of cell-phone exposure on salivary melatonin and cortisol levels. It is possible that the eight males selected for the experiments were low secretors; their nocturnal melatonin levels were only about half the values typically measured in saliva during the acrophase. Burch et al. (2002) performed two studies of melatonin metabolite excretion in male cell-phone users. In one study (77 subjects), there was a linear trend of decreasing melatonin metabolite excretion across categories of increasing cell-phone use. In another study (149 subjects), there were no significant changes. More recently, Wood et al. (2006) suggested "there could be an effect on melatonin onset time" due to mobile-phone use, but there was no significant effect on total melatonin metabolite concentration measured in urine. After shut-down of a short-wave broadcast transmitter, Altpeter et al. (2006) reported a slight increase in melatonin excretion in study volunteers. The authors noted, however, lack of exposure blinding may have affected the results.

De Seze et al. (2001) summarized research of mobile phone RFE exposures and the endocrine system; the authors noted no significant effects. For studies relating to RFE and reproductive hormones, see section "Reproductive endocrinology" above.

Stroke and hematoma

Hocking (1998a) recruited cell-phone users to report symptoms presumed to be associated with such use. Most responders related unpleasant sensations. One woman associated the onset of a sub-arachnoid hemorrhage to a phone call. Hocking (1998b) also reported a woman who experienced "the onset of right-sided pain in the head and became semiconscious after 10 min use of an analog phone; subsequently an intracerebral hematoma was diagnosed." He pointed out that these two cases did not prove a causal relationship. It is interesting to note that Parmar (2002) coined the phrase "telephone stroke" and attributed one case that occurred after a conventional phone call to compression of the ipsilateral vertebral artery.

Hematological changes

Pak (2001) reported that workers exposed to RFE showed "peripheral blood changes: cytopenia, hemoglobin decrease, lower red blood cell (RBC) and white blood cell (WBC) counts, increased RBC with basophilic granularity, WBC metabolism alteration (higher acid phosphatase and myeloperoxidase activity), disordered lymphocytes subunits (T-helpers, T-suppressors) ratio and T- and B-cells numbers." Details of methods and findings were not given in the English abstract.

Blood levels of free radicals

Moustafa et al. (2001) reported that cell-phone RFE exposure resulted in the generation of free radicals, subsequently increasing peroxidation in the plasma of human subjects. Decreases in the activities of superoxide dismutase and glutathione peroxidase in erythrocytes were found. RFE "exposure" consisted of each subject having "the phone in his pocket in standby position with the keypad facing the body" for 4 h. Since there were no "sham exposures," it is difficult to evaluate these findings. There was no indication of a standardized time-of-day exposure and the possible effects of circadian variations in blood or plasma peroxides and superoxide dismutase in humans (e.g., Suplotov and Barkova (1986), Luo et al. (1997)) were not discussed.

Fasciitis and dermatitis

Monfrecola et al. (1999) presented a case report of a man with exposure to 10 GHz RFE. The authors noted, however, that the amount of exposure was difficult to determine. They referred to the exposure as being "well below the permissible exposure level." A mild erythema and a mild burning sensation on the skin were reported; they disappeared within 1 and 3 months after exposure, respectively.

Pereira and Edwards (2000) gave an account of the first case known in the world literature of nodular fasciitis in the deep lobe of the parotid gland. Since the patient was a telephone engineer, the authors were suspicious of an association with higher-than-normal use of cell phones.

Strobos et al. (2001) reported a case of dermatitis "caused by" RFE. The patient, however, had an implanted neurostimulator; the reaction appeared to be related to electrical current being passed through the skin during transcutaneous nerve stimulation. Although Morris et al. (2001) described a case of dermatitis "caused by electromagnetic radiation," the case was associated with direct contact with electrical current. Seishima et al. (2002) found that contact dermatitis in cell-phone users was related to chromium plating on the phone surface (and not to RFE).

Effects on hearing or vestibular system

Meric et al. (1998) reported a higher incidence of hearing loss in 31 workers and family members living in quarters at a radio-broadcasting station than in 30 controls. This effect was presumed to be due to a microwave auditory phenomenon. The authors, when referring to control subjects, stated "special attention was paid in terms of age, sex, type of working ... and working period ... to avoid selection bias." With the limited information available, however, it is difficult to make strong conclusions.

Kellényi et al. (1999) reported that cell-phone exposure resulted in a 20 dB hearing deficit in the 2–10 kHz range. The authors assumed that the effect was due to (a) local heating, (b) ionic membrane shifts, and (c) acute biochemical changes. There was no evidence, however, to support claims of these mechanisms.

In one study, 30 volunteers with normal hearing were exposed to cell phones for 10 min, and evoked otoacoutic emissions were measured before and after exposure (Ozturan et al., 2002). No measurable changes were detected and none of the subjects reported deterioration in hearing level. In a more recent study (Uloziene et al., 2005), another 30 volunteers were exposed to 900 and 1800 MHz RFE from mobile phones for 10 min.There were no significant effects on hearing threshold levels (measured by pure-tone audiometry) or transient evoked otoacoustic emissions (i.e., no measurable hearing deterioration). In another investigation, on the basis of audiometric evaluations, mobile-phone users exhibited a mild hearing loss, compared with non-users (Garcia Callejo et al., 2005).

Pau et al. (2005) applied a simulated Global System for Mobile Communication (GSM) signal (889.6 MHz) to subjects' ears, while performing video nystagmography. No nystagmus was observed. The same research group found no effects of such RFE on auditory functions of either the cochlea or brainstem (Sievert et al., 2005). Two other groups of investigators reported no significant effects of either 900 MHz (Janssen et al., 2005) or 1800 MHz (Parazzini et al., 2005) GSM exposure on distortion product otoacoustic emissions (a measure of the ear's outer hair cell function).

Meo and Al-Drees (2005a, 2005b) performed questionnaire studies and indicated that "earache, heating around the ear and decreased hearing" was greater in mobile-phone users with duration of calls 10-30 or 60-120 min/day, compared with 5–10, 30–60, or more than 120 min per day. There were no control groups of non-users. Maby et al. (2005) found a difference, due to RFE exposure, in correlation coefficients between spectra of auditory evoked potentials. The authors noted, however, that any relation to effects on health was unknown. Kerekhanjanarong et al. (2005) studied 98 mobile-phone users who were undergoing hearing evaluations. There were no differences in audiograms, or pure-tone and speech audiometry between dominant (in terms of mobile-phone use) versus non-dominant ears. Mora et al. (2006) reported no changes in transient evoked otoacoustic emission or auditory brainstem response in healthy men exposed to 900–1800 MHz mobile-phone RFE.

Chromosome aberrations

Lalić et al. (2001) reported a higher frequency of chromatid breaks and acentric and dicentric fragments in peripheral blood lymphocytes of individuals working at radio-relay stations (presumed to be exposed to high levels of RFE) than in controls. These controls, however, were "historical controls" taken from previous unrelated studies. Duration of employment under conditions of RFE exposure did not correlate with the total number of chromosome aberrations. The authors acknowledged that possible confounders included stress, disturbance of neuroendocrine homeostasis, and changes in circadian rhythm. They suggested that changes in melatonin levels due to light deprivation "probably potentiate the toxic effects of" RFE. There is no evidence, however, to support such a claim.

Estecio and Silva (2002) reported significantly higher frequencies of anomalous metaphases in blood lymphocytes from persons presumably exposed to RFE from VDUs. There were no significant differences in mitotic or cellular proliferation indices compared with those from controls. Verschaeve (2005) suggested that studies of chromosome aberrations or micronuclei in peripheral blood lymphocytes taken from subjects with long-term RFE exposure are inconclusive, due to insufficient sample size, lack of consideration of potential confounders, and inadequate dosimetry. In a comparison of blood samples from radio-field engineers versus controls, Maes et al. (2006) found no significant differences in sister chromatid exchanges or chromosomal aberrations. There was, in fact, a trend toward less genetic damage in RFE-exposed subjects.

Stoupel et al. (2005a) found a negative correlation between natural RFE emission (as measured by 2800-MHz solar radio flux) and the incidence of Down syndrome (a year after the RFE measurements).

Suicide

Numbers of suicides were strongly inversely correlated with solar radio flux (Stoupel et al., 2003, 2004, 2005b).

General health effects

Cellular-phone use did not significantly affect serum prostate specific antigen levels in men (Simsek et al., 2003). In another study, television station workers, presumed to be exposed to RFE, exhibited lower overall mortality rates (Solenova et al., 2004). The lack of consideration of obvious sources of bias in worker populations, however, make such studies of questionable value in terms of RFE.

Degrave et al. (2005) found that the all-cause mortality rate was significantly lower in military conscripts who served in battalions with anti-aircraft radars versus controls (age-standardized mortality ratio 0.80; 95% CI 0.75–0.85). Interpretation is difficult since no specific causes of death were reported. No data could be collected regarding actual exposure levels.

A summary of original studies of RFE effects on other systems is presented in Table 5, with this author's opinion of potential effects on health.

Atmospheric RFE

"Sferics" is a shortened term for "atmospherics," which include natural electromagnetic emissions in the ionosphere, caused by lightning during thunderstorms. The predominant frequencies of these emissions are in the extremely low-frequency and VLF ranges. The current paper covers only publications focusing on VLF (i.e., in the RFE range) effects.

Schienle et al. (1998) suggested that VLF sferics could affect the "somatic and emotional well-being of humans, sometimes referred to as weather sensitivity symptoms or meteoropathy." Houtkooper et al. (1999) reported a negative correlation between performance on an extrasensory perception task and VLF sferics activity around the time of the task. Potential confounding factors such as other associated meteorological phenomena (e.g., humidity, air temperature, atmospheric pressure, rainfall, wind speed, pollen levels), however, were not accounted for. The original results were not replicated in subsequent studies (Houtkooper et al., 2001).

Schienle et al. (1999a) studied 32 "subjectively weather-sensitive women suffering from migraine attacks and/or tension-type headaches." The investigators reported that exposure to VLF sferics resulted in EEG changes, but did not induce headache symptoms. In another study (Vaitl et al., 2001a, b) (*note*: duplicate publications as defined by Lundberg (1993)), VLF sferics activity was possibly correlated with migraine incidence during the autumn. The authors concluded that whether sferics and migraines "are directly associated with each other or if the relationship is mediated by other factors cannot be solved by the present investigation." In contrast to the autumn seasonal results above, tension-type headaches were associated with air temperature and atmospheric pressure during the summer, but not with sferics. Walach et al. (2001) measured the intensity and frequency of VLF sferics in an area where patients lived, and compared those results with the incidence of headaches. Only one patient was determined to be "sensitive" to sferics.

Stark et al. (1998) reported no effects of simulated VLF sferics on reaction time in 64 subjects. In an extensive study (5040 responses in 63 subjects), Klöpper et al. (2001) found no evidence that subjects could consciously perceive simulated VLF sferics. Schienle et al. (2001) noticed slight differences in EEG of subjects exposed to simulated VLF sferics (compared to controls), but no effect on subjective state; sferics could not be perceived.

A summary of original studies of atmospheric RFE effects is presented in Table 6, with this author's opinion of potential effects on health.

General reviews of RFE health effects

Repacholi (1998) reviewed research, including epidemiological studies of RFE, and concluded that they did not substantiate claims of adverse health effects. De Seze (1998b) noted that, although low-intensity RFE could cause biological changes, there is no evidence from epidemiological studies or human exposure experiments to suggest an actual health risk. Knave (2001) reviewed health outcomes of exposures to RFE (and lowerfrequency electromagnetic fields) and concluded that more epidemiological and experimental research was needed. Krewski et al. (2001a, b) observed that epidemiological studies did not support hypotheses of associations between RFE exposure and risk for cancer or reproductive effects. The authors found no evidence of established adverse health effects of non-thermal levels of RFE.

Rossignol (1997) referred to a publication (Goldsmith, 1996) as representing "an excellent case study of microwave exposure directed at US Embassy staff in Moscow during the 1970s." Hyland, (2000) cited Goldsmith (1995) as showing "Soviet irradiation of western embassies" with RFE, "done with the express intention of inducing adverse health effects, was quite successful." The suggested effects included changes in blood cell counts. Details of misconceptions presented in the referenced articles have been discussed previously (Jauchem, 1998).

Litvak et al. (2002) reviewed human and epidemiological studies of cancer, reproduction and development, the nervous system, and cardiovascular effects of 300 Hz-10 MHz electromagnetic fields. They concluded that any effects were generally of low magnitude and "not of clear health significance." Röösli et al. (2003)

Reference	Population	Reported effect
Hormones		
De Seze et al. (1998a)	Cell-phone users	No changes in serum adrenotropin and growth hormone; \downarrow thyrotropin at only one sampling point
Mann et al. (1998b)	Male subjects	Slight, transient, ↑ in plasma cortisol
Daşdağ et al. (1999)	Radio and television technicians	↑ Blood triiodothyronine, tetraiodothyronine, and
		thyroid-stimulating hormone
De Seze et al. (1999)	Male subjects	No change in circadian profile of melatonin
Radon et al. (2001)	Normal subjects	No effect on salivary melatonin or cortisol
Vangelova et al. (2002)	Satellite-station operators	↑ "Variability of catecholamine secretion"
Bortkiewicz et al. (2002)	Normal subjects	No effect on melatonin level
Braune et al. (2002)	Normal subjects	No changes in serum epinephrine, norepinephrine,
2100110 00 ull (2002)		cortisol, or endothelin
Burch et al. (2002)	Male cell-phone users	↓ Melatonin metabolite excretion; but, in larger study, no change
Jarupat et al. (2003)	Female subjects	↓ Salivary melatonin
Bergamaschi et al. (2004)	Vendors, operators, and network	↓ Thyroid stimulating hormone
	technicians	¥;
Vangelova and Israel	Broadcast-station operators with	↑ Cortisol, epinephrine, and norepinephrine
(2005)	presumed "high-level" RFE exposure	
Wood et al. (2006)	Normal subjects	No effect on total melatonin metabolite concentration
		measured in urine
Altpeter et al. (2006)	Broadcast-station workers	Lower melatonin excretion
Stroke		
Hocking (1998a)	Cell-phone users	Unpleasant sensations
flocking (1996a)	Cen-phone users	Supreasant sensations
Hematological changes		
Pak (2001)	Workers "exposed to RFE"	\downarrow Hemoglobin; – red blood cells with basophilic
		granularity
Blood levels of free radicals		
Moustafa et al. (2001)	Normal subjects	↑ Generation of free radicals
	-	'
Effects on hearing or vestibular		
Meric et al. (1998)	Workers and family members living at	↑ Hearing loss
	radio-broadcasting station	
Kellényi et al. (1999)	Cell-phone users	20 dB hearing deficit in 2-10 kHz range
Ozturan et al. (2002)	Volunteers with normal hearing	No effects on evoked otoacoustic emissions; no
		hearing deterioration
Uloziene et al. (2005)	Volunteers with normal hearing	No effects on hearing thresholds; no hearing
		deterioration
Pau et al. (2005)	Normal subjects	No nystagmus
Sievert et al. (2005)	Normal subjects	No effects on auditory functions of either the cochlea
		or brainstem
Janssen et al. (2005)	Normal subjects	No effects on distortion product otoacoustic
		emissions (measure of ear's outer hair cell function)
Parazzini et al. (2005)	Normal subjects	No effects on distortion product otoacoustic
		emissions (measure of ear's outer hair cell function)
Meo and Al-Drees	Mobile-phone users	Decreased hearing greater with some durations of
(2005a, b)		calls versus others
Maby et al. (2005)	Healthy and epileptic patients	Difference in correlation coefficients between spectra
V and have a		of auditory evoked potentials
Kerekhanjanarong et al.	Mobile-phone users undergoing hearing	No differences between dominant versus non-
(2005)	evaluations	dominant ears in audiograms, or pure-tone and
	TT 1/1	speech audiometery
Mora et al. (2006)	Healthy men	No changes in transient evoked otoacoustic emission or auditory brainstem response
		or auditory brainstem response

Table 5.	(continued)
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Reference	Population	Reported effect
Chromosome aberrations		
Lalić et al. (2001)	Workers at radio-relay stations	↑Chromatid breaks, and acentric and dicentric fragments in lymphocytes
Estecio and Silva (2002)	Persons presumably exposed to RFE	↑ Anomalous metaphases in exposed to RFE from
	from VDUs	lymphocytes; no change in mitotic or cellular proliferation indices
Stoupel et al. (2005a)	Offspring of subjects	↓ Incidence of Down syndrome
Maes et al. (2006)	Radio-field engineers	No changes in sister chromatid exchanges in peripheral blood lymphocytes
Suicide		
Stoupel et al. (2003, 2004, 2005b)	General population	↓ Suicide rate
General health effects		
Simsek et al. (2003)	Male subjects	No effect on prostate specific antigen
Solenova et al. (2004)	Television station	↓ Mortality workers
Degrave et al. (2005)	Military recruits who served in battalions with anti-aircraft radars	↓ Mortality

Table 6. "Atmospheric RFE"

Reference	Population	Reported effect
Houtkooper et al. (1999)	Persons reportedly having extrasensory perception (ESP) abilities	↓ Performance on ESP task
Houtkooper et al. (2001)	Persons reportedly having ESP abilities	No effects on ESP task
Schienle et al. (1999a)	"Subjectively weather-sensitive women suffering from migraine attacks and/or tension-type headaches"	Changes in EEG, but no headaches
Vaitl et al. (2001a, b)	Patients	↑ Migraines in autumn
Walach et al. (2001)	Headache patients	95% of patients not "sensitive;" one patient "sensitive" to RFE
Stark et al. (1998)	Normal subjects	No effect on reaction time
Klöpper et al. (2001)	Normal subjects	No conscious perception of RFE
Schienle et al. (2001)	Normal subjects	No perception of RFE; slight difference in EEG

suggested that "the existing scientific knowledge base is too limited to draw final conclusions on the health risk from exposure in the low-dose range." Habash et al. (2003) indicated that, on the basis of epidemiological and clinical studies, "evidence for a causal relationship between RFE and adverse health effects is limited." Srebro and Dziobek (2003), in a review, simply focused on the biophysics related to potential effects of RFE.

Ahlbom et al. (2004) focused on cancer, adverse reproductive effects, and cardiovascular disease, and reported no convincing or consistent evidence of associations with RFE. Kundi (2005) criticized those authors for not considering consequences of sources of bias on risk indicators. Ahlbom et al. (2005) disagreed, and claimed that they "did consider these at some length" in their review. Although the authors had mentioned possible biases, discussion of potential consequences of these biases on risk estimates had not been included (Ahlbom et al., 2004).

Regarding potential adverse effects of mobile-phone RFE, Rumiantsev et al. (2004) contended that the available data were too contradictory to arrive at a final conclusion. Feychting et al. (2005), found "no persuasive data suggesting a health risk" of RFE, but noted "this technology is constantly changing and there is a need for continued research on this issue." In one recent review of exposure to mobile phones, Karger (2005) concluded there was a lack of harmful non-thermal effects. The only established risk was an "indirect effect" of increased vehicle collisions due to use of a mobile phone while driving. Munshi and Jalali (2002) also found this effect.

Wood (2006) suggested that available evidence "falls short of what is normally required to establish a causal link" between RFE exposure and health effects. It is difficult, however, to determine what evidence investigators would deem sufficient to support a causal relationship.

Non-English-language articles

Non-English-language articles for which no abstracts were available (or for which abstracts contained minimal information that was insufficient for meaningful interpretation) and that were not previously mentioned in the current paper include: Bernhardt (2005), Dodina et al. (2004), Drecun (2003), Eliseev and Romanov (2004), Galeev (1998), Gavriutin (1995), Grigoriev (2001, 2003, 2005a, b), Kliap and Kuryk (2002); L'Abbate and Terrana (2001), Li et al. (2004), Liu (2002), Liutov et al. (1998), Marchenko (1998), Petrowicz and Friedrich (1998), Rager and Sakal (2001), Santini et al. (2001, 2002b), Schienle et al. (1999b), Schweisfurth (2002), Simonenko et al. (1998), Suvorov et al. (2001, 2002a, 2b), Trabacchi (2002), and Tynes and Hannevik (2001).

Concluding remarks

Limitations of science regarding RFE health effects research

General problems of studies of RFE-exposed populations have been discussed in detail by Chou (2003). The problems include selection bias, lack of proper exposure assessment, recall bias, selection of appropriate controls, and confounding factors. Masley et al. (1999) reviewed cell-phone safety in general and reiterated the challenges of exposure assessment and potential confounders in epidemiological research regarding this issue. In addition, the simultaneous testing of multiple hypotheses must be interpreted with caution.

Problems due to publication bias include overestimation of risks and easier publication of statistically significant than of non-significant results. These problems can only be solved by more journals publishing null results (Knight, 2003). Some editors have encouraged this, with either whole journals (Pfeffer and Olsen, 2002) or special sections of journals (Shields, 2000) being devoted to null results. It is important, however, to provide sufficient experimental details to allow interpretation of negative results (Knight, 2003). Fortunately, recently there have been great improvements in this aspect relative to RFE studies.

Simply relying on interviews to assess RFE exposures can result in misclassification and biased risk estimates (Behrens et al., 2004). Schüz and Mann (2000) have

pointed out "the pace of radio infrastructure development is ... such that today's measurements are unlikely to be good proxies for either past or future exposures." Larsen and Skotte (1994) noted that, "in the light of the problems in exposure classification, the epidemiological research may not be conclusive, and attempts should be made to improve the methods." In general, output powers of mobile phones are considerably higher in rural areas (where there are fewer base stations) than in more densely populated areas (Lonn et al., 2004). Thus using distance from base stations (e.g., Santini, 2002b, Santini et al., 2003a, b) as the main exposure metric (without quantitative assessments of individual RFE exposures) may be misleading. In addition, Burch et al. (2006) recently found that factors such as (a) line-of-site, (b) reflection from local buildings, terrain, or vegetation, and (c) temporal variability of RFE could have important effects on residential exposure to RFE from broadcast antennae, apart from distances.

In any epidemiologic study, the balance of withinand between-person variation in exposure must be considered (Loomis and Kromhout, 2004). In addition Von Elm and Egger (2004) have pointed out that even relatively satisfactory studies may result in misleading findings if relevant confounders are not even identified, let alone measured precisely. Most authors do not explain their choices of confounding variables (Pocock et al., 2004). Multiple statistical testing of hypotheses can also lead to a high probability of reporting associations that are false. These factors would appear to be particularly important in studies of RFE.

Since many reported "effects" were within normal physiological ranges, relevance to health hazards is uncertain. Repacholi (2001) stressed the importance of distinguishing between biological effects and adverse effects on health. Havas (2000) presented an interesting and thought-provoking commentary on "cultural bias" (associated with different scientific disciplines), which can affect the extent of evidence generally required before a scientific judgment is considered convincing. This aspect is particularly worthy of note regarding RFE research.

The use of cell phones is considered by some to be a unique risk since exposure to such RFE "is not detected with the senses" (Passchier, 2000). Some authors are convinced that adverse effects of RFE are ubiquitous (see, e.g., Saunders, 2003). Hefer (2005) included mobile-phone use as one example of how (a) statistically significant results and (b) theories to explain such results, are not always sufficient for proof of a causative effect. Repacholi (2001) made the cogent observation that "newly published scientific research is sensationally reported without qualification from the results of previous studies."

Regarding power-frequency electric and magnetic fields, Swanson and Kheifets (2006) suggested that, if

no plausible mechanism exists to explain potential effects, "the level of proof required from the epidemiology and other strands of evidence" is higher than it might be otherwise. The same may be true for potential effects of low-level RFE. A number of toxicologists, however, will disagree with this idea. Although great progress has been accomplished in developing mechanistic models for toxicology (Conolly, 2002), only a small number of environmental or occupational factors have been linked to such models for adverse effects.

This author has attempted to avoid an inordinate amount of interpretive bias (Kaptchuk, 2003) in this review. Hopefully, the "significance and limitations of the data" (Rier, 2003) of the studies have been discussed appropriately.

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