News from Science

The following paragraphs refer to recent original scientific studies investigating effects of mobile radio frequency fields. Publications were selected by the author, Prof. Roland Glaser, due to his personal judgement of relevance.

Roland Glaser

What does epidemiology say so far on potential risks of exposure to occupational and normal life radio frequency fields? Five members of the ICNIRP's Standing Committee on Epidemiology did an extensive review off all to-date published epidemiological studies on a potential assocation between fields in the frequency range of 100 kHz to 300 GHz and diseases or disturbances of well-being of exposed persons in a detailed survey. The data is compiled in 9 tables, subdivided according to the type of exposure and symptoms, and is thoroughly discussed. Results: The authors conclude that to-date published epidemiological findings do not provide any consistent or convincing evidence revealing a causal relationship between radio frequency field exposure and any serious health damages. On the other side they concede that available studies are too often compromised by flaws and gaps to exclude such effects with certainty. This is shown in detail in the survey: First, there is the lack of dosimetric evaluation. The simple subdivision of the examined population according to their distance from the transmission mast is shown to be as dubious from a physical point of view as questions regarding phoning habits included in other studies. There is then the well-known problem of small samples: If an average of 10 to 15 persons out of 100,000 persons develop brain tumors per year, numbers are not sufficient for a statistically valid survey. The numbers for other diseases are more or less the same. Only common complaints, such as headache, sleep disorders, fatigue etc., do occur much more often. However, they are more difficult to detect objectively, and the studies pretending to be able to correlate these disturbances of human well-being with field exposure, are error-prone. One of many possible error sources are, of course, so-called confounders – a mass of mostly unidentified causes behind health disorders, which are legion in our modern world; conditions that objectively confound epidemiological studies and cannot be fully avoided, even by the most diligent work. Other limitations are: a lack of data on long-term exposure, ie the actual incubation period of hypothetical effects is unknown, and a lack of long-term studies in children. A general problem is that there is no evidence yet in biophysics as to what types of influences we should be looking for. Epidemiological studies account for irrational fears in the general population, and not for scientific hypotheses. As can be expected, the recommendation is to continue research – how could it not? –, but not without considering past flaws and with the highest possible degree of objectiveness and accuracy *(Ahlborn, A.; Green, A,; Kheifets, L.; Savitz, D., and Swerdlow, A.: Epidemiology of health effects of radiofrequency exposure. En-*

vironmental Health Perspectives 112, 1741-1745. 2004).

Do mobile radio fields produce oxidative stress? Cells of animals get their energy from "burning", ie "breathing", or in chemical terms: the oxidation of energetic nutrients. This is a dangerous process insofar as the fire in the oven may not spread to the furniture by flying sparks! These "sparks" are various interim products formed during oxidation. Sometimes they are also summarized ROS = reactive oxygen species. Their concentration and localization is kept in check by an elaborate system of cellular regulation. Disturbances of this system can lead to oxidative stress and may have serious consequences. There are many causes of such disturbances, e.g. rises in temperature and, as various authors suggest, perhaps also radio frequency field exposure. This hypothesis is validated by a working group in a cell culture of mouse macrophages (J774.16 cell ine). The cells were exposed to a CDMA field (847.74 MHz) and a FMSW field (835.62 MHz), each with 0.80 +/- 0.13 W/kg, for 20 to 22 hours. Both unaffected cells and cells chemically exposed to oxidative stress suboptimally or optimally prior to the test (by gamma-interferon or a bacterial lipopolysaccharide) were examined. Then both the occurrence of oxygen species and the activation of the cellular defense system as well as cell survival were investigated. An influence of radio frequency fields could not be found. Oxidative stress was neither induced in unaffected cells, nor was the chemically induced stress in any way affected by the fields. The conclusiveness of these negative findings is statistically confirmed *(Hook, G.J.; Spitz, D.R.; Sim, J.E.; Higashikubo, R.; Baty, J.D.; Moros, D.G.; Roti Roti, J.L.: Evaluation of parameters of oxidative stress after in vitro exposure to FMSW- and CDMA-modulated radiofrequency fields. Radiat. Res. 162, 497-504. 2004).*

New Swedish study investigating the correlation between cancer of the auditory nerve and mobile phone use. The issue has already been studied in the USA and in Denmark *(Christensen et al. 2004, see: NEWS FROM SCIENCE, 3/2004).* There is now a new Swedish study which critically reviews the publications of Hardell from the years 1999 and 2002 *(see: NEWS FROM SCIENCE, 1/2003)*, also based on Swedish data. 148 clinically recorded and clearly diagnosed cases of acoustic neuroma in the regions Stockholm, Göteborg and Lund (total number of inhabitants 3.1 millions) are evaluated and compared to 838 control persons. During personal conversations with educated staff extensive data are recorded: phoning habits (since when? which device? metropolitan or rural? hands-free device? how often? right or left?), age, sex, social class, etc. DECT phone use was also recorded (OR=0.7, confidence interval: 0.4 to 1.2), but not further considered in the following. 148 cases are reduced to very small numbers very fast by being divided into specific groups. In contrast to Hardell, who was criticized for the methodological flaws of his study, the authors conclude that there is no association between mobile phone use and acoustic neuroma detectable (OR=1.0, 95%-confidence interval: 0.6 to 1.5). However, an increased risk for persons with more than 10 years of mobile phone use cannot be excluded. But as the respective calculated OR=4.8 is based on the evaluation of only 10 persons, this conclusion is very unreliable (confidence interval: 1.1 to 20.1). According to the authors, this value could mean both that a corresponding incubation period of the tumor is required or that it is due to the stronger fields of the old analogue technology. Results could have been falsified also by recall bias: patients tend to exaggerate possible causes, especially when recalling situations 10 years after. This concerns e.g. information on the frequency of mobile

phone use. A general flaw of such surveys can result from the fact that mobile phone users perceive hearing losses that are due to this disease earlier than others so that the cancerous development is diagnosed faster and more often. The widespread habit to listen to extremely loud noise is seen as a possible cause of this type of cancer (confounder) *(Lönn, St.; Ahlbom, A.; Hall, P., and Feychting, M.: Mobile phone use and risk of acoustic neuroma. Epidemiology 15, 653-659. 2004)*.

What are potential biological effects from millimeter waves? Time and again, there are publications examining this frequency range which has been used for therapeutical applications in the former Soviet Union. From experiments with nose-only exposure of mice the authors conclude that peripherous nerve ends are stimulated at a penetration depth of less than 1 mm in tissue, and, subsequently, killer cells are activated in the blood via unknown mechanisms. Regrettably, there is no comparison between influences ofweak infred radiation and 42.2 GHz fields (31 mW/cm², 30 min) *(Makar, V.R.; Logani, M.K.; Bhanushali, A.; Kataoka, M.; Ziskin, M.C.: Effect of millimeter waves on natural killer cell activation. Bioelectromagnetics 26, 10-19. 2005)*.

Is melatonin synthesis changed by exposure to mobile radio fields? Though there are several studies on this issue already, with negative findings, the hypothesis claiming alterations for the alternate current frequency range, even though it was not confirmed, is still cited. Recent experiments with mice exposed during dark hours, from eight o'clock to midnight (when most phone calls are made in Japan!) to the 1439 MHz of a TDMA signal (brain SAR = 7.5 W/kg, average SAR= 1.9 to 2 W/kg) could show that there was no change in the melatonin or serotonin contents, neither of the blood nor of the pineal organ, compared to controls, and neither immediately after switching off the field nor 6 hours later *(Hata, K.; Yamaguchi, H.; Tsurita, G.; Watanabe, S.; Wake, K.; Taki, M.; Ueno, S., and Nagawa, H.: Short term exposure to 1439 MHz pulsed TDMA field does not alter melatonin synthesis in rats. Bioelectromagnetics 26, 49-53. 2005)*.

Do mobile radio fields promote brain tumor growth? Aside from epidemiological studies, long-term animal experiments are required to provide an answer to this question. Neither the study of Adey et al. from 2000 *(Cancer Res. 60, 1857)* nor that of Zook and Simmens published one year later *(Radiat. Res. 155, 572, see also NEWS FROM SCIENCE 3, 2001)* could find an influence from radio frequency radiation in long-term experiments with rats. There is a new comprehensive study from Japan investigating the issue. As in the two previous studies, brain tumors were induced in rats by ENU (ethylnitrosourea) injections. The substance was given to 103 pregnant rats; the 551 newborns were then used in experiment. 16 to 30% of the animals developed brain tumors after about 2 years of living, due to the ENU treatment of their mothers. Exposure to 1.439 GHz of a TDMA signal (90 min/day, 5 days/week, with a SAR in the brain of 0.67 and 2 W/kg) was irrelevant. There was no evidence of any other differences between exposed and sham-exposed animals either. There was a distinctly slower growth rate only in cage control rats which had been exposed to irradiation as well as after sham-irradiation *(Shirai, T.; Kawabe, M.; Ichihara, T.; Fujiwara, O.; Taki, M.; Watanabe, S.; Wake, K.; Yamanaka, Y.; Imaida, K.; Asamoto, M., and Tamano, S.: Chronic exposure to a 1.439 GHz electromagnetic field used for cellular phones does not promote N-ethylnitrosourea induced central nervous system tumors in F344 rats. Bioelectromagnetics 26, 59-68. 2005)*.

Chromatin changes in healthy and „electrosensitive“ persons after weak exposure to 50 Hz and 915 MHz? Lymphocytes taken from blood samples of seven healthy volunteers and as much self-reportedly „electrosensitive“ persons were examined for their response to a two-hour exposure to 50 Hz magnetic fields (0.015 mT) and GSM signals of a mobile phone (915 MHz, 37 mW/kg). An influence on cell apoptosis was found neither after 24 nor 48 hours. The evidence of the expression of a breast cancer-specific gene through reactions with an anti-53BP1-antibody failed to reveal significant results. Only the ACDT technique (Anomalous Viscosity Time Dependies), repeatedly used by Belyaev, but rejected by other authors as being entirely unspecific, shows differences immediately after exposure (at 50 Hz – $p<0.015$, at 915 Mhz – $p<0.004$) that vanish though after 2 hours and are interpreted as chromatin condensation. The authors conclude from this that their tests have proven effects of stress for weak 50 Hz and mobile radio fields, similar to those caused by heat shock. Significant differences between control volunteers and “electrosensitive“ persons are not derived from results. The introduction and the discussion included in the paper do not comply with usual scientific standards. Both paragraphs only cite authors who claim to have found positive effects, regardless of whether they have been criticized for obvious methodological flaws a long time ago, or whether their results have been disproved by more recent experiments. Critical reviews or publications reporting vain attempts to reproduce their results are simply ignored. Also, an explanation why the authors postulate a high frequency specificity of effects, on the other side confusing the entirely different interaction mechanisms of 50 Hz and 915 fields, lacks *(Belyaev, I.Y.; Hillert, L.; Protopopova, M.; Tamm, C.; Malmgren, L.O.G.; Persson, B.R.R.; Selivanova, S.; Harms-Ringdahl, M.: 915 MHz microwaves and 50 Hz magnetic field affect chromatin conformation and 53BP1 foci in human lymphocytes from hypersensitive and healthy persons. Bioelectromagnetics 26, 173-184. 2005).*

Do mobile phones really activate heat-shock proteins? Recently, a number of authors have published data on the expression of heat-shock and other proteins claiming to have found so-called “non-thermal“ cell reactions to weak mobile radio fields. Ian Cotgreave from the Department of Biochemical Toxicology at the Karolinska Institutet (Stockholm) discusses these results and correlates them with a cellular adjustment and regulatory system responding in this manner to many chemical and physical parameters. He adds that, generally, there is a regulated balanced flow of protection and repair proteins inside the cell, including heat-shock proteins (Hsp), ie they constantly develop and are broken down. Valid conclusions on alterations can only be drawn when considering the entire process, instead of looking at one changed expression. 13 publications with part negative, part positive results on Hsp expression caused by radio frequency fields are summarized in a table and discussed in detail. The results are contradictory, to some extent unconvincing methodologically, and in general difficult to compare due to the differences between single test conditions, such as exposure parameters and cell types. To-date conducted animal tests could neither provide convincing evidence for such an effect, at least for mobile radio field intensities. Using modern analysis techniques, the number of publications dealing with gene activation and expression of proteins with various cell biological functions is increasing at present. Even though results do not yet present a consistent picture, the question of mechanisms which may be responsible for such reactions and, above all, of the biophysical sense of the

term "non-thermal" is crucial. There are controversial opinions as to whether radio frequency field absorption can possibly lead to an increase in the thermal vibration of certain proteins and, thus, to a conformational change affecting their function. Finally, the author makes recommendations concerning future research. Besides the necessity to use clean application apparatuses, which is a matter of course, the recommendations mainly refer to the standardization of cells. Primary human cell cultures are to be preferred over cancer cell lines and animal models. Furthermore, analysis methodologies have to be improved, including conclusive statistics. Without additional research on molecular processes occurring during RF field absorption, it is not possible to make assertions on frequency and modulation specificities and dose-effect curves. Conclusions on health effects can only be drawn and a scientific basis of limits found, if effects are put into an organismic context *(Cotgreave, I.A.: Biological stress responses to radio frequency electromagnetic radiation. Are mobile phones really so (heat) shocking? Arch. Biochem. Biophys. 435, 227-240. 2005).*

Discussion about limits with Ron Petersen of ICES goes on. In the previous issue we reported on the critique by Martin Blank and Reba Goodman regarding the conclusions on harmlessness drawn by the members of the International Committee of Electromagnetic Safety (ICES), especially of the Subcommittee SC4 concerning limits, presented in the 2003 special edition of Bioelectromagnetics, and the response of its President, Ron Petersen. He rejected the critique, pointing out that limits cannot be legitimated by unconfirmed hypotheses, but only on the basis of scientific facts. Cindy Sage of the Sage Association, California, now enters the debate, claiming that the definition of health-damaging effects applied by the SC4 members was to narrow, far more narrow than the WHO's definition. Also, the old allegation that the committee members were paid by industry and thus were not independent resurfaces. Petersen responds to the second allegation only insofar as to request evidence of hitherto possibly ignored scientific data. Otherwise there is no problem for him to accept the WHO's definition of health risks, including not only diseases but also "discomfort", by defining health as a state of "complete physical, mental and social well-being" (who of us does feel "healthy" in this sense?). Although the reviews in the aforementioned supplement cited authors with results raising concerns regarding such health risks, none of these results met the required conditions of scientific reliability. Assessments included in the reviews reflected not only the opinion of the ICES and its more than 100 international experts; moreover they agreed with the conclusions of more than 17 other expert bodies, including the WHO *(Sage, C.: Comment on "Reviews of the effects of RF fields on various aspects of human health" [Bioelectro-magnetics Supplement 6 (2003)]. Bioelectromagnetics 26, 157-168. 2005; Petersen, R.: ICES reply. Ibid. 159-160).*

Biochemical alterations in the rat brain after acute exposure to GSM 900 MHz. At 15-min exposure of the head of rats to a 217 Hz pulsed intense 900 MHz field, significant biochemical alterations can be found in various neuroreceptors. The average SAR in the brain is 6 W/kg, the maximum value 15.5.+/-5 W/kg (why is there no dispersion for the average value?). Appearingly, there is no effect on the animals' behavior (locomotion test right after exposure). The authors surmise that measured effects are caused by modifications of different phospatases. They exclude thermal effects, based on temperature estimates and the regulatory role of blood circulation (but how is it activated?). They point out that these results cannot necessarily be extrapolated to humans, due to the

high intensity used in this test, and with regard to geometric differences *(Mausset-Bonnefont, A.L.; Hirbec, H.; Bonnefont, X.; Privat, A.; Vignon, J.; de Sèze, R.: Acute exposure to GSM 900 MHz electromagnetic fields induces glial reactivity and biochemical modifications in the rat brain. Neurobiology of Disease 17, 445-454. 2004)*.

Daily use of mobile phones does not impair cognitive performance. To date, opinions on whether fields emitted by a mobile phone held to the ear have an influence on memory function, attention capacity, reaction rate etc., are contradictory. Tests have until now been performed during field exposure. There is now an investigation available where 28 out of 55 persons of both sexes, aged between 18 and 40 years, non-intensive users of mobile phones (less than 10 min a day), were asked to sit down for two hours, five days a week in a chair, to watch television and hold the mobile phone in the usual position to their ear, the arm supported on the armrest, under exposure conditions (exposure: 900 MHz, 217 Hz pulsed, 0.54 W/kg average SAR measured in a phantom head). The rest of the group held a device that was switched off. Various psychological tests accompanied this strictly double-blinded experiment extending over 45 days. None of the 22 different test procedures could find differences between exposed and non-exposed persons. Possible errors, which could have led to the contradictory results of other authors, are discussed. As a main cause, the possibility that tests were blinded, but not double-blinded is mentioned *(Besset, A.; Espa, F.; Dauvilliers, Y.; Billiard, M.; de Sèze, R.: No efffect on cognitive function from daily mobile phone use. Bioelectromagnetics 26, 102-108. 2005)*.

Do mobile radio fields influence the behavior of rats? An endless story! We reported several times on the experiments performed by the working group around Henry Lai (Univ. of Washington, Seattle), who claimed to have found proof of an influence on the behavior of rats, not only at exposure to 60 Hz magnetic fields but, already in 1994, also to mobile radio fields *(Bioelectromagnetics 15, 1995)*. He sees subsequent own studies (see NEWS FROM SCIENCE, previous issue) as confirmation and denies that other findings from vain attempts to replicate his experiments are valid *(Bioelectromagnetics 26, 81. 2005)*. However, he stands alone with this opinion, since several other groups have vainly tried to reproduce effects *(Sienkiewicz et al.: Bioelectromagnetics 21, 151. 2000; Dubreuil et al.: Behav. Brain Res. 145, 51. 2003; Cobb et al.: Bioelectromagnetics 25, 49. 2004)*. There is another study available now, presented by a French working group, where the same field parameters were used (2.45 GHz, 500 Hz pulsed, 0.6 W/kg). Effects were not found. However, the experiment was not about capacity of orientation and memory. Instead, the degree of anxiety of the animals was tested using methods of behavioral research. The animals can select between two options, ie four maze arms: two of them allowing them to hide, and two open channels promising activity. The urge to hide increases with the strength of lighting (2.5 to 30 lux) and, on the other side, can be reduced by pharmaceuticals (diazepane). Both influences are used as positive control. A significant change in this behavior could not be observed, when the animals were exposed to the aforementioned field for 45 min, prior to the test *(Cosquer, B.; Galani, R.; Kuster, N.; Cassel, J.C.: Whole-body exposure to 2.45 GHz electromagnetic*

fields does not alter anxiety responses in rats - a plus-maze study including test validation. Behav. Brain Res. 156, 65-74. 2005).

900 MHz GSM fields cause first steps in apoptosis in white blood cells; but 1800 MHz do not? In issue 4 (2004), we reported on a study conducted at the University of Bologna *(Capri et al.: Rad. Res. 162, 211, 2004),* where lymphocytes from human donor blood, compared to controls, showed a certain intensification of the first steps in apoptosis from the influence of pulsed, but not unpulsed 900 MHz fields, after treatment with an apoptosis stimulator (dRib). However, the authors think that a verification of results is necessary. This recommendation deserves special attention, also considering another paper of the same group reporting similar investigations with 1800 MHz. Although the SAR was increased from 0.07 W/kg to 1.4 to 2 W/kg, no influences were found this time around. The authors draw the right conclusion, namely that the findings obviously depend on many factors that are difficult to control, and experiments therefore have to be designed due to highest quality standards *(Capri, M.; Scarcella, E.; Bianchi, E.; Fumelli, C.; Mesirca, P.; Agostini, C.; Remondini, D.; Schuderer, J.; Kuster, N.; Franceschi, C.; Bersani, F.: 1800 MHz radiofrequency (Mobile phones, different Global System for Mobile communication modulations) does not affect apoptosis and heat shock protein 70 level in peripheral blood mononuclear cells from young and old donors. Intern. J. Radiat. Biol. 80, 389-397. 2004).*