

"Influence of low and high frequency electromagnetic fields on spontaneous leukaemia in AKR/J mice"

and

"*in vivo* experiments on exposure to the high frequency electromagnetic fields of mobile telecommunication. B. carcinogenesis"

Prof. Alexander Lerchl's contribution to the German Mobile Telecommunication Research Programme:
The effect of chronic exposure to athermic GSM and UMTS mobile communication signals
on the development of spontaneous lymphatic leukaemia in AKR/J female mice

A critical commentary by Franz Adlkofer

During a seminar in Stockholm in October 2010 Eric van Rongen, member of the International Commission on Non-ionizing Radiation Protection (ICNIRP), presented a list of papers with which he pretended to prove that mobile communication radiation does not constitute a risk for cancer development. Included in his list were two papers by Prof. Alexander Lerchl's team at the private Jacobs University Bremen, both resulting from the German Mobile Telecommunication Research Programme (DMF) which was jointly funded by the telecommunication industry and the German Government between 2002 and 2008:

Sommer AM, Streckert J, Bitz AK, Hansen VW, Lerchl A (2004) No effect of GSM-modulated 900 MHz electromagnetic fields on survival rate and spontaneous development of lymphoma in female AKR/J mice. BMC Cancer 4:77

Sommer AM, Bitz AK, Streckert J, Hansen VW, Lerchl A (2007) Lymphoma development in mice chronically exposed to UMTS-modulated radiofrequency electromagnetic fields. Radiat Res 168:72-80

The *German Competence Initiative* asked me once again for a commentary on these two papers. Regarding Prof. Lerchl's position in the German Commission on Radiological Protection (SSK) of the Federal Office for Radiation Protection (BfS), they wished to learn if his scientific failure as demonstrated in the 'melatonin project' (<http://www.pandora-foundation.eu>) was a single error or if the suspicion of poor scientific qualification can be further substantiated. Should the latter apply, the German Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) were confronted with the question if it is willing to take over the responsibility for Prof. Lerchl's ongoing funding by the BfS as well as for his mission as head of the Committee on Non-ionizing Radiation within the SSK.

Aim of the studies

The aim of the two research studies from which the two papers emerged was to investigate, if chronic exposure to GSM or UMTS mobile communication signals can influence onset and development of cancer in AKR/J mice. In these animals malign lymphomas develop due to a certain genetic modification, starting at the fourth month of age and killing nearly all of them in their first year of life. The Specific Absorption Rate (SAR) for the whole-body exposure of the mice was fixed at 0.4 W/kg, a value five times higher than the currently valid whole-body exposure limit for humans. The results were thought to increase our knowledge whether high-frequency electromagnetic fields can influence the development of cancer in the hematopoietic systems. The BfS as well as the authors rightly regarded the current state of knowledge as being insufficient and the available data as being contradictory.

Methods

During the GSM research study - carried out between October 2002 and September 2004 - 160 mice were exposed for 24 hours/day to GSM-like 900 MHz electromagnetic fields at a SAR of 0.4 W/kg. In a second, identical exposure unit placed in the same room 160 animals were kept as a sham-exposed control.

For the UMTS research study - carried out between October 2003 and April 2005 - again two groups of 160 mice each were used. One group was exposed to UMTS-like 1966 MHz electromagnetic fields at a

SAR of 0.4 W/kg, while the other one acted as sham-exposed control. This time 30 – or as mentioned elsewhere – 33 additional animals were kept as a cage control in the same room. It is emphasized that the experiments were *blinded*, that means the persons in contact with the animals (scientific staff, technical assistants, animal care) did not know which group of animals was exposed and which one was sham-exposed. As explicitly declared, the blinding code was disclosed only after the statistical evaluation had been completed.

To detect signs of disease at a rather early stage the mice were examined daily or – as mentioned elsewhere – every one or two days. Once a week, the weight was controlled. At the same time, the animals were palpated in order not to miss the onset of lymphoma. At the first sign of disease (lymphomas, shortness of breath, weight loss, or ruffled fur) animals were killed humanely. The same was done with the few still healthy animals at the end of the radiation period. At this date, the mice of the GSM study were about 46 weeks old, while the ones of the UMTS study were 43 weeks old. **In both papers we find the remarkable sentence that the experiments carried out do not allow any statement on the onset or on the course of the tumour incident, as in such experiments animals had to be killed and examined at certain time points without considering clinical symptoms. I will come back to this!**

Summary of the results

1) Results of the GSM study

From the final report to the BMU (http://www.emf-forschungsprogramm.de/forschung/biologie/biologie_abges/bio_040_AB_b.pdf) we learn that altogether no harmful effects could be detected when the AKR/J mice were exposed to a GSM-like 900 MHz radiation under the conditions mentioned. Statistically significant differences regarding the median survival time, that is the lifespan reached by 50% of the animals, were not observed between exposed and sham-exposed animals. Accordingly, at the end of the experiment neither the frequency of lymphomas nor the number of animals still alive differed. The only statistically significant difference was an increased relative body weight of the exposed animals compared to the sham-exposed ones. The body weight was not given in absolute values, since the differences were very high within both groups. In the discussion of the report it is stated that the electromagnetic fields applied in the experiment do *with a high degree of significance* not influence the onset or the course of the disease. In the conclusion of the report it is stated that even results obtained with high SAR values do not point to negative effects of the radiation *so that with the general restriction to transfer animal experiments to the situation of humans there is no reason to lower the current safety limits for the whole-body exposure.*

In the peer-reviewed paper in *BioMed Central Cancer* the results which were presented in the final report as mentioned above are confirmed and complemented. In the exposed group, the first mice died of lymphomas 60 days after exposure started, in the sham-exposed group this happened after 88 days. The median survival time was 190 days in the exposed group and 183 days in the sham-exposed group, the median time when lymphomas were palpated was 183 and 193 days, respectively. In both cases differences were not statistically significant. From these results it was concluded that the hypothesis of a cancer development in the hematopoietic system of genetically pre-disposed mice as a result of long-term exposure to high-frequency electromagnetic fields, such as from mobile phones and base stations, is not supported. Correctly, it is added that with these findings radiation exposure being a risk factor for other forms of cancer cannot be excluded.

2) Results of the UMTS study

According to the final report for the BMU (http://www.emf-forschungsprogramm.de/forschung/biologie/biologie_abges/bio_060_AB.pdf) the only significant difference between exposed and sham-exposed animals was the fact that with 28 (17.5%) more exposed than with 14 (8.8%) sham-exposed animals reached the end of the exposure term without showing detectable disease symptoms. The possibility that this might be a result of the exposure is not forgotten to mention. However, the number of diseased animals, the course of the disease and the severity did not differ between the two animal groups. The same was true for body weight and blood picture. Based on these findings the authors concluded that (a) their results *do not point to any harmful effect from month-long exposure to UMTS fields at a value five times higher than the whole-body exposure allowed for humans (80 mW/kg)*, (b) the study did not show results *that give reasons to lower the current safety limits for whole-body*

exposure, and (c) the experiments carried out are a significant contribution to health care, because possible health risks should be recognized before the frequency of diseases in the population is rising. The authors are obviously convinced that their results exclude any potential risk to the health of people from UMTS radiation even if – as they say – convincing data from epidemiological studies on direct effects on humans are not available yet. UMTS is still a very new communication system.

The presentation of the results in the peer-reviewed journal *Radiation Research* differs from the final report only in so far as it is not mentioned anymore that the number of animals that survived in a healthy state till the end of the experiment was significantly higher in the exposed than in the sham-exposed group. Opposite to the previous report, the authors claim that at the end of the experiment the percentage of healthy mice in the exposed group did not differ significantly from the percentage of healthy mice in the sham-exposed group. This is illustrated with $P=0.055$, a value above the level of significance. The median survival time of exposed animals was 172 days and of sham-exposed ones 165 days, the median time when lymphomas were first observed was 141 and 149 days, respectively. In both cases the differences were not statistically significant. Corresponding to this, the number of diseased animals and the severity of the disease did not differ between the experimental groups, too. The increase in body weight of the mice did considerably vary between 23.5 g and 53.3 g, however, without being different in the two groups. The pathological and histopathological findings together with the blood picture indicated that all animals with the exception of two had developed lymphomas. Of the original 350 mice four died spontaneously while 303 were killed before the end of the experiment because of their critical state of health.

Commentary

I should mention at the outset, that the two studies do not nearly meet the claim to have contributed anything to the knowledge on risk assessment of tumour development in the hematopoietic system through mobile communication radiation. Regarding the missing link to real life any scientific significance of the results has to be rejected. There are mainly two reasons that enforce such an explicit statement, namely the general overrating of animal experiments on cancer development through mobile communication radiation and - in the presented studies - especially the strong suspicion that results have been manipulated due to subjective influences on the experimental procedure.

1) The relevance of animal experiments to clarify health risks of mobile communication radiation

According to Prof. Lerchl the AKR/J animal model has turned out to be perfectly suited to carry out experiments on the carcinogenic effect of mobile communication radiation. The mice are easy to handle, do not show any or little aggression, and are quite homogenous with regard to the investigated parameters. The high number of animals, 160 in each group, would have been appropriate to provide evidence that the negative results stand firm. However, Prof. Lerchl's esteem for this model seems to be mainly based on the fact that the results of the experiments do seemingly meet his expectations. This will be discussed later. Why the contribution of experiments with animal models to the clarification of a cancer risk through electromagnetic fields is rather limited, show the following considerations:

- The metabolism of humans and animals can be compared - based on the different genetic constitution and the different epigenetic processes - only with some reservations. This is especially true for the AKR/J mice that die at an early age due to a dominant gene causing a special form of leukaemia. This gene does not exist in humans at all or is ineffective in humans. From the beginning, this distinction alone prevents that the results of the described animal experiments can be transferred to humans. Although Prof. Lerchl is aware of this problem, he fully ignores it in his conclusions.
- While investigating the carcinogenic potential of a substance or a physical agent, the animals normally receive very high doses because it is assumed that short-time exposure with a high dose leads to results comparable to those of a long-term exposure with a low dose. Therefore, dose increase is used in order to justify first a reduced number of test animals and in addition a minimal exposure time. This is quite different from the real life situation with humans. However, the procedure prevents that the animal study is impracticable due to technical and financial limitations. Regarding the thermal effects of high-frequency electromagnetic fields, this approach cannot be chosen in mobile communication research as test animals would die of overheating.

- To overcome this problem mobile communications research turns more and more to models with animals that are treated with a carcinogenic substance in addition to exposure or – as in our case – to genetically modified animals with a pre-disposition of cancer. The constraint that risk assessment is further complicated with this element of uncertainty has to be accepted.
- It is true that animal studies dealing with carcinogenic effects of high-frequency electromagnetic fields did produce controversial results. However, studies with a negative outcome do in no way devalue a single study with a positive outcome as long as this study has been properly planned and properly carried out. But this was certainly not the case with Prof. Lerchl's studies.

Indeed, there are such positive studies. The well-known Repacholi study is mentioned by Prof. Lerchl, but dismissed. A more recent study with mice, too, carried out by the Fraunhofer Institute for Toxicology and Experimental Medicine in Hannover and not known to Prof. Lerchl before 2008 shows that UMTS radiation has only a low genotoxic effect leading to tumour initiation, but a strong epigenetic effect leading to tumour promotion. A significant increase of the tumour rate in liver and lung of mice, treated prenatally with the carcinogenic compound ethylnitrosourea (ENU), above the effect of ethylnitrosourea alone was observed after UMTS radiation with a flux density of 4.8 W/m^2 , that is half of the current safety limit for base stations (*Tillman et al. (2010) Indication of co-carcinogenic potential of chronic UMTS-modulated radiofrequency exposure in an ethylnitrosourea mouse model. Int J Radiat Biol 86(7):529-41*).

Obviously, the results derived from this properly planned and properly carried out study cannot be brought in line with Prof. Lerchl's view. His view, however, would lose any significance, should we discover that his experiments do not stand up to scientific criticism because of improper design and improper handling.

2) Consequences of the research plan on the result of the animal experiments

a) The research plan allows the manipulation of the results in any desired direction

In the GSM final report to the BMU, Prof. Lerchl declares that his research project is based upon the instructions of the BfS which said that animal studies are necessary to test the effects – among other things – of electromagnetic fields (900 MHz GSM) in one and the same animal model, the AKR mice. These mice would develop spontaneous leukaemia and would, therefore, be a good model to investigate possible initiating or promoting effects of exposure to this kind of radiation. In the UMTS final report, Prof. Lerchl mentions as an additional aim of the investigation, to clarify *if chronic exposure to fields of the mobile communication standard UMTS influences the leukaemia rate or the promotion of solid tumours in animal models*. In both peer-reviewed papers, we find the sentence "the present experiment does not allow any conclusions about tumor onset or the kinetics of tumor development, since for such type of study animals would have to be sacrificed and examined at fixed intervals irrespective of clinical symptoms". If this is true - and it is without any doubt - the conclusion must be that the results described in the reports do not meet the requirement that initiation and course of leukaemic process have been correctly picked up, since they were obtained by means of an unreliable procedure. Therefore, the claimed reliability of the results is pretended. This means that both research studies should never have been approved and carried out in their present form.

We can only suspect why the authors - also knowing better - did not carry out their research study in a way necessary to really gain new knowledge. The assumption that Prof. Lerchl deliberately selected a research approach that allowed him to determine the course of the study according to his expectations is probably the most plausible explanation. In both studies, the GSM and the UMTS one, the majority of the animals were sacrificed during the exposure period. Killing was done when mice showed first signs of disease (lymphoma, shortness of breath, loss of weight, or ruffled fur). Since the signs of disease develop – as everybody knows - slowly for quite a while the killing was dependent on the investigator's subjective impression. It must have been clear to Prof. Lerchl, who was responsible for the studies, from the beginning that he might have to take into account critical questions because of this unusual procedure. However, he obviously believed that he could counter with the statement that the experiments were *blinded* and the related code was disclosed only after the statistical evaluation had been completed. And not knowing which of the two groups was exposed and which one was sham-exposed the investigator would indeed be forced to act objectively.

b) Obviously it was made use of the possibility to manipulate

For scientists with laboratory experience, it is obvious that the indispensable *blinding* of the experiments in both studies was in no way guaranteed regarding the experimental conditions, which could not have been simpler. The assumption that a fairly intelligent staff member should not have been able in the course of about 40 weeks to find out in which of the two exposure units the exposed and in which one the sham-exposed mice were housed can be called the crown of simplicity. And there is indeed evidence that the experiments were carried out without *blinding*. These are the reasons:

In the UMTS study, the number of mice supposed to have reached the end of the exposure period in a healthy state was in the exposed group with 28 (17.5 %) animals considerably higher than in the sham-exposed one with 14 (8.8 %) animals. Prof. Lerchl declared this difference in a presentation within the DMF consortium with $P < 0.01$ as being highly significant, and in his UMTS final report for the BMU he described it at least as being significant, but did not indicate anymore the level significance. Based on this finding he suggested at both opportunities a possibly positive effect of mobile communication radiation. Strangely, in the peer-reviewed UMTS paper he did not mention this allegedly positive effect anymore. Despite the same number of animals, this time he calculated a P-value of 0.055. According to Prof. Lerchl's understanding of statistics, this level of significance was obviously not worth a further discussion. He might have been right, because there is indeed an explanation for this phenomenon. Obviously, the investigators assessed the state of health of the exposed animals as being better than the state of health of the sham-exposed ones because this subjective expectation was in line with the prevailing view in Prof. Lerchl's laboratory.

This assumption is supported by the fact that in both studies the median survival time of the exposed mice was with 190 and 172 days, respectively, clearly - though not significantly - higher than in the sham-exposed group, where it was with 183 and 165 days, respectively. The supposed positive effect of mobile communication radiation is, however, not in line with the median time for the development of lymphomas that were diagnosed after the animals had been sacrificed. Since the median time for tumour development in both studies was with 183 and 141 days clearly, but not significantly shorter in the exposed group, respectively, than with 193 and 149 days in the sham-exposed one, respectively, suspicion of a tumour accelerating effect of the mobile communication radiation cannot be dismissed. The opposite course of the median survival time and of the lymphoma development time in both studies might be pure coincidence, but most probably it is further evidence of data manipulation resulting from the invalid blinding procedure.

The alleged positive effect of mobile communication radiation, deviated from the higher number of exposed animals that apparently did reach the end of the exposure period in a healthy state, was also discussed by Prof. Lerchl in an internet forum as being inconvenient for mobile communication critics, but nevertheless true. The telecommunication industry might have appreciated this. In reality, however, it has to be revealed that we are dealing with *junk science*. Whether Prof. Lerchl finally recognized his failure and, therefore, refrained from presenting the allegedly positive effect of mobile communication radiation in his peer-reviewed UMTS paper or whether someone forced him to withdraw from this nonsense idea, is not known yet. Prof. Lerchl is known to accuse any scientist of producing *junk science* whenever his/her research results contradict his own. This should at least be mentioned in this context.

Conclusions

Aim of the investigations was to find out whether exposure to high-frequency electromagnetic fields constitutes a risk for cancer development in the hematopoietic system. The two final reports to the BMU and the subsequent peer-reviewed papers give the impression that this question has successfully been answered. But in fact this is not true. The repeated statements that no effect could be observed speaking in favour of a carcinogenic potential of high-frequency electromagnetic fields and the conclusion that there is no necessity to lower the safety limits are both fully misguided and not at all supported by the reported results. Based on the way how the experiments were carried out it is indeed possible that the effects of radiation escaped notice in the exposed animal. The slightly faster development of lymphomas in both studies would support such an assumption. But it seems equally possible, that no effect of radiation would have been detected, even if the experiments were carried out properly. Because of the distinct genetic predisposition for leukaemia the risk might hardly be increased during the short lifespan of the animals by this kind of radiation.

Both papers by Prof. Lerchl's team point at a series of further shortcomings. For example, it is rather unlikely that the extreme difference of the body weight can primarily be ascribed to pathogenic processes, particularly, as the animals were already sacrificed at first signs of disease. A probable explanation could be seen in the housing conditions of the animals that point at considerable stress among the mice (6-7/cage). Conspicuous in the peer-reviewed UMTS paper are also the figures regarding the frequency of metastatic infiltrations of the brain and the meninges, which are not in line with the ones presented in the final report to the BMU. Because of the scientific insignificance of the findings altogether which is the sequence of how the studies were planned and performed, it is not necessary to go into more details. However, it is impossible to ignore serious doubts on the scientific qualification of Prof. Lerchl, who was responsible for the planning and realization of the worthless studies in question.

The publication of the kind of papers submitted under the responsibility of Prof. Lerchl indicates that the peer-review process in scientific journals has become a farce as far as the mobile communication research is concerned. Of course, this is in contrast to the opinion of Prof. Lerchl who considers the entry of his papers in the scientific literature as a quality feature of his work. Since the BfS financed this kind of work, which is good enough only to prove the still miserable state of science in mobile communication research, and since it is not shy of using these worthless findings to play down possible health risks of the mobile communication radiation, doubts must come up whether this Office fulfils the prerequisites of a reputable scientific institution. The close collaboration with Prof. Lerchl for years now strengthens these doubts. Obviously, nobody in the Office seems to be able to recognize the immense shortcomings in Prof. Lerchl's research, let alone the impression that he much more supports the interests of the telecommunication industry than those of the people in Germany for whom he is responsible. Obviously, the severe criticism of the BfS by the German Council of Science and Humanities (Wissenschaftsrat) in May 2006 turns out to be true.

If Prof. Lerchl would have openly admitted to be a researcher in the service of the mobile communication industry as many others with a similar view are, I would not have bothered to question the results he describes in his publications and the conclusions he draws. However, being the head of the Committee for Non-ionizing Radiation in the SSK of the BfS, Prof. Lerchl has decisive influence on how our citizens will be protected from the possible health risks of mobile communication radiation. Instead of doing so, he takes advantage of their dependence on experts in dealing with new scientific data with which he pretends a safety of the respective technology not justified regarding the current state of knowledge. To a lack of scientific qualification comes obviously a lack of scientific integrity and both together make Prof. Lerchl's position as the people's protector from risks of radiation intolerable. The BMU must see itself in front of the question how long it will still support this disastrous, the interests of the mobile communication industry servicing research which is to a great deal funded by the tax-payers. For sure, it is not without reason that the people in Germany just started to demonstrate their loss of confidence in the governmental decision-makers.