

**Comments from Annie J. Sasco, MD, DrPH, SM, MPH, retired Director of Research at the INSERM (French NIH) and former Unit Chief at IARC-WHO, France**

I am a physician and a scientist having spent the past 35 years working on the epidemiology of cancer and to a lesser extent other chronic diseases. I graduated as an MD'78 from the University of Bordeaux, France, also getting several specialized qualifications (hygiene and social medicine; occupational medicine; spatial and aeronautical medicine). As I needed a more scientific education in Public Health in order to practice real population health, I came to the Harvard School of Public Health and successfully completed 3 Harvard degrees: Master of Public Health'79, Master of Science in Biostatistics and Epidemiology'80 and Doctor of Public Health in Epidemiology, Biostatistics and Evaluation'86. While being a Harvard Teaching Fellow for a few years I joined the INSERM (French NIH) and decided to work on secondment from INSERM at the International Agency for Research on Cancer – World Health Organization (IARC-WHO) for 22 years, including 9 as Head of Program and then Chief of Unit of Epidemiology for Cancer Prevention and 2 as Acting Chief of the WHO Program for Cancer Control. I later returned to an INSERM Research Unit at the University of Bordeaux.

Over the decades, my focus switched from behavioral to environmental risk factors as I was confronted by the huge increase in cancer occurrence worldwide, not only in terms of burden of disease, but also in incidence rates after due consideration to the changes in population size and age structure. As these increases cannot be linked to genetic changes, nor only to behavioral or life-style modifications, and after taking into account the role of screening, earlier detection, improvement in diagnosis and better registration of cancer, increases in the occurrence of many cancers in different parts of the world have to be recognized as a true fact, including in Europe childhood cancer. The most logical potential explanation of these increases is the change in our environment in the past 50 to 70 years. Although some carcinogens always existed, the presence of chemical and physical carcinogens in the air we breathe, the water we drink, the food we eat and objects of daily living exploded. While I recognize the exact quantification of the attributable role of these contaminants in cancer occurrence remains debatable, I contend it is scientifically arguable a non neglectable part may be due to these pollutants. One of the most ubiquitous exposure to physical agents is the exposure to ELF and EMF which has been one of the most rapidly expanding, in particular over the past 30 years and this is accelerating. Soon the exposure to RFR will be so widespread that it will be also impossible to find unexposed human populations and human epidemiology will face an unprecedented challenge.

This is why I want to truly congratulate the NTP program for having conducted the experimental study on exposure of rats and mice to RFR. This very nicely complements what is already known from epidemiology. Briefly stated, although epidemiology is often presented as showing limited evidence of carcinogenicity for RFR, my contention is that most epidemiological studies and in particular case-control studies while finding no overall increased risk when comparing exposed to unexposed do find increased risk in the group where it is expected to be found, namely the most heavily exposed, whatever the exact definition is, varying from study to study. This is for example the case of the Hardell studies conducted in the Nordic countries, the Interphone international study and the CERENAT study in France. Such a consistent finding should not be attributed to chance, but rather should be seen as what one can expect, especially with a relatively short study time scale as far as cancer induction period at the population level is concerned. In this context, the NTP study brings

additional evidence on the carcinogenicity of RFR in experimental animals. This effect is mainly seen in rats and in male rats more than in females whereas findings in mice are more equivocal.

My questions are the following:

- Why was the choice made of intermittent exposure with short cycles? Was it to limit any thermal effect?
- Considering the ANFR French report recently released reveals some SAR levels higher than what was tested in the NTP study when measured on skin contact, do not you think that the results at 6 W/kg are particularly relevant?
- Some of the results are not statistically significant due to the relatively small number of animals involved. Yet, that does not mean they should be ignored. Larger studies will be more likely to turn out statistically significant results and in any event statistical significance is just one aspect of the evaluation of the relation between exposure and disease. Biological significance and concordance of results between humans and animals clearly reinforce the strength of the evidence of carcinogenicity.
- The way the report presents the levels of evidence is unclear. Could you please specify for example how to separate limited from equivocal evidence? As a comparison the way to define the levels of evidence in the IARC Monograph preamble are clearly defined.
- The fact that higher SAR are considered to be related to mortality should be underscored as it may be pertinent to human experience
- Could you please expand on the increase in whole body temperature as experienced by animals with whole body exposure as compared to localized increases as in humans with only part of their body exposed when using or carrying a phone?
- Could you please carry out a proper statistical analysis with due correction for survival when looking at the overall tumor burden in exposed versus unexposed rats?
- The fact that survival was lower in unexposed rats is a surprising factor, comforted by the fact that survival was lower than in historical controls. For future studies, it could be advisable to have an unexposed group larger than each of the exposed ones, in order to build in a more stable reference population. In the present case could there be some metabolic pathway involved, the exposed animals having in the perinatal and lactational periods a lower body weight?

## Conclusion

Almost 10 years ago, Dr David Servan-Schreiber and myself co-wrote what is known as the 20 doctors and scientists appeal (Paris, France, June 2008), calling on people to use their cell phones in a cautious way. We considered at that time there was already enough evidence to advise people to follow 10 measures: when calling, keep their phone as far away from their body as they could; use the loud speaker; keep conversations short; switch to the use of a corded landline when possible or send text-messages rather than talk; avoid any use of cell phone by children and young adolescents; keep the phone away from the bed or turned off at night; when not in use avoid carrying the phone directly on your body or in your pocket, in particular for pregnant women; change side when talking and avoid using the phone when the reception is poor; choose a phone with the lowest SAR; try to

stay at a distance from people using cell phones, in particular in closed settings such as cars, trains or elevators.

In the past 10 years many more studies came out. Some may consider there is still not enough evidence. How many more deaths should we wait for? Even if some consider there is still doubt, what is the risk of being cautious? All the recommendations we stated are still valid, even more so than before and the results of the NTP study are one more step in the direction of advising precaution. As a doctor, I never forget I took the Hippocratic oath and I obey to the rule “Primum non nocere” (First, do no harm).