

Hold the phone?

Abstract. Cellular phones have become indispensable personal communication devices used by over 2 billion people worldwide. Few of these users realize that they may be sacrificing their health for this convenience, since researchers have suggested that the electromagnetic radiation emitted by cell phones could be linked to an increased likelihood of developing certain cancers. The experimental and epidemiological studies examining this correlation have produced conflicting results. While very little consensus has been reached, this review article seeks to provide an overview of mobile phone technology, recent research into the link to disease proliferation, current public policy practices, and areas of further research.

Cellular phones have revolutionized interpersonal communication. In the past fifteen years, cell phones have transformed from exorbitantly-priced brick-sized devices to compact, economical gadgets used by over 2 billion people worldwide (1). They not only make it possible to contact anyone, anywhere, but can simultaneously function as a camera, planner, address book, web browser, music player, or even television set. Unfortunately, some scientists warn that the electromagnetic waves produced by mobile phones may have serious health consequences. While the FCC and FDA, which share the responsibility for regulating the U.S. wireless phone industry, have claimed that “there is no scientific evidence that proves that wireless phone usage can lead to cancer or a variety of other problems,” (2) new studies have forced them to re-evaluate their guidelines. This review provides an overview of mobile phone technology, recent research into the link to disease proliferation, and current public policy practices.

The risks of exposure to electromagnetic fields were first publicized in the late 1970s by a Colorado study that linked magnetic field exposure from power lines to the development

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of childhood leukemia (3). These results have since been invalidated; researches have noted that the study had an unblinded assessment of exposure and that the Earth's natural magnetic field is at least two magnitudes larger than the fields created by any power line or electric device (3). In addition, the survey was repeated in 1997 by the National Cancer Institute (4), and showed very little correlation between magnetic-field levels and the risk for developing acute lymphoblastic leukemia (ALL).

However, concerns related to the health effects of electromagnetic radiation have re-emerged with the relatively recent cell-phone boom. Cell-phones are essentially radios that work by sending and receiving signals made of radio-frequency (RF) energy, which is a type of electromagnetic radiation (5). The phone contains a low-power transmitter that translates the sounds waves from your voice into a sine wave. The sine wave is then sent out into space using an antenna and picked up by a receiver in a cell-phone tower.

All cell-phones emit a small amount of non-ionizing radiation from the antenna, which is placed very close to the head when the phone is in use (4). RF radiation can damage tissue by heating it; the eyes and testes are particularly vulnerable. High doses of radiation can also have enough energy to break DNA bonds (3). However, the amount of radiation emitted by cell phones is relatively low so the temperature increase of the tissue in the side of the head closest to the cell phone is thought to be less than 0.1°C (5). Still, very little is known about how much radiation is potentially harmful and whether long-term exposure to this radiation can be linked to cancer, brain tumors, Alzheimer's, Parkinson's, fatigue, or headaches.

In recent years, many cellular, animal, and epidemiological studies investigating this link have been conducted by researchers around the world. These studies have generated conflicting conclusions. The following summaries are intended to provide an overview of the

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research that has been done in the field to promote discussion and consensus on future research directions.

Cellular Studies

Cellular studies provide a unique opportunity to conduct carefully controlled experiments which exclude environmental effects and other complicating issues that arise when studying live animals.

Researchers have used cellular studies to validate phenomena observed on the macro scale. Even exposing human skin fibroblasts, which are connective tissue cells, to the RF radiation from a global system for mobile communications (GSM) phone for only one hour showed increased expression of signal transduction genes, cell growth inhibitors, and apoptosis-controlling genes (6). These gene expression changes caused more DNA to be synthesized and showed that electromagnetic fields (EMF) can induce biological alterations in human cells.

Marinelli *et al.* applied the same procedure to study of cultured acute T-lymphoblastoid leukemia cells (CCRF-CEM) *in vitro* to examine the suspected link between high-frequency EMF exposure and leukemia (7). They exposed the cultured cells to unmodulated 900 MHz EMF for both short and long periods. Short exposure times of 2-12 hours induced DNA breaks and early activation of pathways which lead to programmed cell death. Long exposure times of 24-48 hours activated genes that enhance cell survival and sped-up cell replication. Thus, the data suggests that high frequency EMF exposure can enhance the survivability of cancer cells and potentially promote tumor formation.

This experiment was recently repeated by Merola *et al.* using a neuroblastoma cell line, which are cells that can give rise to extracranial childhood cancer (8). They exposed the cells

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for 24, 48, and 72 hours to the same 900 MHz EMF used by Marinelli *et al.* and studied the proliferation, differentiation, and apoptosis processes occurring in the cell line. The study concluded that even 72 hours of continuous exposure did not significantly change the activities of the neuroblastoma cells.

Several explanations could account for the dramatic discrepancy in the results. Both experiments had thorough controls so the difference is not likely to be attributed to a faulty experimental setup. For example, Marinelli *et al.* used a temperature control to exclude any thermal effects and a sham exposure to observe non-radiated cells. Merola *et al.* controlled for the effects of other cellular components by testing the interaction of the RF exposure, which is a type of EMF, with chemical exposure to retinoic acid or the apoptotic inducer camptothecin. However, the dissimilar results could be attributed to the different cells tested, since leukemic cells are known to be very susceptible to high-frequency EMFs exposure while neuroblastoma cells are not. But this explanation is merely a hypothesis and both Merola and Marinelli *et al.* suggest that further research should be done on the effect of EMF exposure on normal cells.

Animal Studies

Even more controversy surrounds the results of animal studies. In 1997, Repacholi *et al.* (9) exposed 100 female transgenic mice -- with a predisposition to developing lymphoma -- twice a day for 30-minutes, every day for 18 months. They used 900 MHz electromagnetic fields (EMF) with specific absorption rate (SAR) values between 0.008 (very low) and 4.2 W/kg (very high.) The transgenic mice had almost twice the risk of developing lymphoma than the control mice. Hence, the study concluded that people with genetic predispositions to developing lymphomas could be increasing their risk by RF exposure.

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These results caused widespread interest and generated considerable discussion on the health effects of EMF. Several studies sought to repeat Repacholi's results while correcting some of the study's weakness. In 2002, Australian researchers working for the National Health and Medical Research Council tested the same hypothesis as Repacholi *et al.* except for a few crucial changes (10). They used a smaller variation in SAR values, standardized their assessment criteria, dissected mice even when they were thought to have no relevant diseases, and exposed the mice to radiation for 6 months longer. Despite these stricter standards and more rigorous testing conditions, the study concluded that the RF-field exposure did not cause an increase in lymphoma.

The study was also repeated by German researchers who exposed 160 mice to 900 MHz EMFs for 24 hours a day, 7 days per week, at an SAR value 0.4 W/kg (11). They collected blood samples from the mice once a week when they were between the ages of 24 and 46 weeks, at which point they were sacrificed and examined. The mice exposed to EMFs had significant weight change compared to the sham control mice, but overall they had similar survival rates and growth patterns. One important note is that the SAR value used (0.4 W/kg) was chosen because it is supposedly five times higher than the limit of whole-body exposure to the general population, though it is significantly lower than the FCC-determined maximum human exposure value of 1.4 W/kg. Despite this, it seems that the newer, more scientifically-sound experiments do not support the original conclusion by Repacholi *et al.*

One final animal study with notable results was conducted by researchers at Columbia University in 2003 (12). They found that exposing fruit flies to a GSM phone for the duration of their 10-day developmental period had dramatic consequences. EMF exposure increased the number of offspring, levels of a heat shock protein, and phosphorylation of a nuclear

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transcription factor. Thus, there is evidence that GSM telephones have more than just thermal influences on living organisms.

Epidemiological Studies

While detailed and controlled experiments using cells and animals give important insight into the molecular effects of EMF, it is difficult to make the logical leap that applies these conclusions to the human body. In order to produce data that can influence lawmakers and provoke change, researchers must conduct detailed and controlled epidemiological studies, which study the causes and distribution of diseases in human populations.

The FDA used data from a study conducted in 2000, which found no association between handheld cellular telephone usage and brain cancer, to create their current guidelines (13). The study collected data from 469 brain cancer patients and 422 control patients regarding the hours per month, total number of years, and lifetime cumulative hours spent using a cellular phone. In hindsight, the study is fundamentally flawed due to the short latency period and small sample size. The mean duration of handheld cellular telephone use was about 2.8 years, which may not be long enough for the RF energy that is absorbed into the biological tissue to cause permanent damage. Also, the majority of case and control patients was over 60-years-old and therefore was less likely to use cellular phone and not representative of the average cellular phone user.

Smaller countries with better records lend themselves to epidemiological studies with very accurate data and huge sample sizes. A particularly striking study conducted in Denmark utilizes the nation's cellular phone user records concurrently with the Danish Cancer Registry to study all phone users from 1982 to 1995. The study of 420,000 cell phone subscribers, about 15% of the adult population, concluded that there was no link between phone use and cancer

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(14). Researchers also did not find an association between the anatomical locations of brain tumors and the region around the ear where the cell phone is generally held, since this area receives the highest levels of radiation. Despite the huge sample size, the study is limited by a short latency period and too few heavy users, which may mask the effects resulting from long-term exposure on slow growing brain tumors. Also, more than 42% of cell phone users were excluded from the study because of a variety of complications and a healthy group effect bias may be skewing the results.

While the Danish study concluded that there was no link between radiation and cancer, Swedish researchers conducted their own study to elucidate the causes of the dramatic increase of Non-Hodgkin's lymphoma (NHL) between the 1960s and 1990s (15). NHL is a cancerous growth of B or T white blood cells in the lymph system. The incidence of NHL has increased because of a rise in various risk factors including organic pollutants and autoimmune diseases. Hardell *et al.*, the Swedish research team who conducted the study, hypothesized that cell phone radiation could be one of these risk factors, citing Repacholi *et al.*'s study demonstrating DNA damage in lymphocytes after EMF exposure. Since about 30% of RF emission during a phone call is absorbed by the skin and subcutaneous tissue in the head and neck, it is possible for circulating blood, which transports B and T-cells, to be exposed and altered by this radiation. Their study verified that digital cellular or cordless phone use increases the risk for T-cell NHL, though the results are inconclusive for B-cell NHL. They also found that the risk increases with increasing latency period.

Many studies, including Hardell *et al.*'s 2005 study, have examined the association between cellular phone use and tumor formation, but few have produced conclusive results due to small sample groups and short latency periods. Building on a previous study, Hardell *et al.*

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developed two new case-control studies that addressed latency period concerns by including 96 cases of people with malignant brain tumors that used cellular telephones for more than ten years (16).

The basic study used a 20-page questionnaire to gather data from about 2,500 cancer patients, including 1,000 with a malignant brain tumor, and 2,500 control subjects that were matched with these subjects by age, sex, and geographic area based on information from the Swedish population registry. The Nordic region was one of the first to embrace cellular phone technology, thus it provides an opportunity to gather data on the long-term health consequences of usage.

The statistical analyses showed that people who used cellular and cordless phones for more than ten years had an increased risk for malignant brain tumors, especially a specific type called high-grade astrocytoma. An especially troubling result was that cellular and cordless phone users under the age of 20 had an even higher risk of developing brain tumors. Since this is the most recent and thorough study conducted to date, it is imperative that the survey is repeated by other researchers and appropriate public awareness campaigns are implemented.

Regulation of cell phone radiation levels

The publication of the study by Hardell *et al.* prompted the FDA to release a statement on April 6, 2006 stating plans to re-evaluate the link between cell phone use and cancer.

The FCC has created safety guidelines for radiofrequency exposure based on research and recommendations by the National Council on Radiation Protection and Measurements and the Institute of Electrical and Electronics Engineers (17). Based on this research, the threshold level of exposure is a whole-body Specific Absorption Rate (SAR) of 4 watts per kilogram and

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cell-phone companies must manufacture phones with an SAR value less than 1.6 watts per kilogram.

The FCC's guidelines on SAR values have not changed significantly since the Telecommunications Act of 1996, and since then there has been evidence to support the harmful health effects of RF exposure. However, in consumer information published in 2003, the FCC still claims that there are no known risks from RF emission exposure and that there is no scientific evidence to show health problems associated with using wireless phones.

In addition to the FCC, the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and other agencies all contribute to the monitoring and regulation of RF radiation in the U.S. Internationally, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) developed world-wide guidelines and the World Health Organization established the International Electromagnetic Fields project to study the health effects of EMF (18). Also, The International Agency for Research on Cancer (IARC), a specialized WHO cancer research agency, is performing a large epidemiological study to investigate the link between cell phones and cancer. Until the results of this study are complete, WHO is enforcing strict adherence to current guidelines, suggesting precautionary measures to the government and individuals, such as avoiding EMF interference and limiting phone use while driving.

Future Research

In order to bring together the varied conclusions reached by the studies discussed in this review, it necessary to develop well-controlled epidemiological experiments coupled with cellular and animal studies, which explain the underlying mechanisms of cellular damage by EMF.

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Future epidemiological and animal studies must implement innovative experimental designs. Current studies are fraught with confounding variables and biases, which are difficult to overcome but crucial to control. The results are also questionable because of the small sample size and short latency period. As more time passes, it will become easier to examine the long-term effects of cell phone radiation but harder to find a suitable control group.

Also, much of research found in the literature merely seeks to repeat previous studies' findings. Rather than wasting time and money on these ventures, scientists should collaborate on larger projects to solve this complex problem in a more methodical manner. The World Health Organization's study seems to be one of the first such attempts and its results are eagerly anticipated. If it is a success, surely more such collaborations will form.

Conclusion

Many cellular, animal, and epidemiological studies conducted over the past ten years have made significant contributions to our understanding of the effects of cell phone radiation. Older reports fail to analyze the long-term effects of RF exposure simply because cell phones have only become widely used in the past decade. While the studies are becoming increasingly precise and scientifically sound, many questions have yet to be answered and there is still no incontrovertible evidence linking high-frequency EMF to cancer. In the meantime, since over 69% of Americans use mobile phones (1), it seems best to err on the side of caution until studies with larger sample sizes, more reliable data, and longer latency periods can generate more conclusive results. Finally, it is imperative for lawmakers and federal regulatory commissions to be aware of the most recent study by Hardell et al. and make decisions accordingly. After all, with 200 million cell phone users in the US alone (1), even somewhat rare adverse health effects can inflict damage on hundreds of thousands of people.

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