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Cellular (Mobile) Telephone Use and Cancer Risk

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HISTORY, DEFINITIONS, SOURCES, AND BIOLOGIC EFFECTS OF RADIOFREQUENCY RADIATION

An anecdotal 1993 United States (U.S.) television report linking a woman's brain tumor with her cell phone use led Congress to urge the National Cancer Institute to conduct epidemiologic research on brain tumor risks associated with cell phone use. Public concerns were driven by the dramatic increase in use of a novel technology and the largely unknown etiology of brain tumors. Cell phones emit radiofrequency energy which is a form of non-ionizing radiation. Electromagnetic radiation includes two major types: ionizing or high-frequency radiation (such as that produced by x-ray machines, nuclear energy, radon and other forms), which has been shown to pose cancer risks, and non-ionizing or low frequency radiation (such as radiofrequency emitted by cell phones, microwaves or radar or extremely low-frequency emitted by power lines and many electrical appliances), which is not established as carcinogenic /1,2/. At high power levels, radiofrequency radiation can cause heating of tissue.

The level of radiofrequency energy produced by cell phones, however, is too low to produce significant tissue heating or an increase in body temperature /1/. The most common use of radiofrequency energy is for telecommunications including AM/FM radios, VHF/UHF televisions, cellular telephones, and cordless telephones, which historically operated at lower radiofrequencies than cellular telephones. Other sources of radiofrequency energy include radar, satellite stations, magnetic resonance imaging devices, microwave ovens, and industrial equipment, all of which operate at higher frequencies than cell phones /1/. Limited numbers of epidemiologic studies that have evaluated cancer risks associated with exposures to radiofrequency energy sources other than cell phones have shown null results or a few inconsistent findings, but often statistical power was insufficient to provide stable risk estimates for brain tumors, leukemia, or other rare outcomes /1/. There is no consistent experimental evidence of carcinogenicity or genotoxicity associated with radiofrequency radiation exposure, and a potential biologic mechanism by which radiofrequency radiation might cause cancer has not been identified /1/.

Patterns and Trends in Cell Phone Use

The number of cell phone users has risen exponentially from 0.3 million U. S. subscribers in 1985 to 119 million in 2000 and 255 million in 2007 /3/. For many subscribers, the average number of hours of cell phone use per month has also increased due to greater frequency and length of cell phone calls. Early cell phones used analog technology, which emitted radiofrequency waves of 800-900 megahertz (Mhz). In the 1990s, digital technology utilizing higher radiofrequencies (ranging up to 2200 Mhz) replaced the analog systems /1/.

Exposure from Cell Phones: How, When, Where, and Amount

A cell phone user's primary source of radiofrequency exposure is through the antenna, which is in the handset. Typically, the user holds the handset next to the side of the head. The

closer to the head, the greater is the radiofrequency energy exposure level, and the further the distance, the lower is the energy level. The intensity of radiofrequency energy emitted by a cell phone depends on the level of the signal sent to or from the nearest base station /1/. When a call is placed, a signal is sent from the antenna of the phone to the nearest base station antenna. The base station then routes the call through a switching center where the call is transferred to another cell phone, the local landline telephone system or other base stations to be transferred to more distant cell phones or landline phone systems. The further the distance between a cell phone antenna and the nearest base station antenna, the higher is the power level necessary to maintain the connection.

For handsets held on the side of the head, there is concern that radiofrequency energy produced by the cell phone may affect the brain and associated structures such as the meninges, the nerve to the ear, salivary and parotid glands /1/. Researchers have therefore investigated whether radiofrequency energy can cause tumors of the brain, the meninges (the membranes that cover and protect the brain and spinal cord), the nerve that supplies the ear, and tumors of the salivary glands and the parotid glands.

A cell phone user's level Of exposure depends on the distance between the phone's antenna and the nearest base station, whether or not a handsfree device is used, the number and duration of calls, the size of the handset, the quality of the transmission, and the amount of cell phone traffic at a given time /1/. Higher radiofrequency energy exposure levels were emitted by analog phones compared to the lower exposure levels emitted by digital phones. The increasing number of base stations has also reduced the distance that signals need to travel between the cell phone and the base station antennas, thereby decreasing the power level needed to maintain the connection /1/.

Why is there Concern that Cell Phones May Cause Cancer?

Cell phone technology is relatively new and is still evolving, so there are relatively few studies that include persons with long duration of use, and few investigations that have included large numbers of early users. Given the dramatic increase in the numbers of cell phone users, the higher frequency of use, the longer average length of phone calls, and the growing numbers of long-duration users, even small increases in cancer or other serious diseases may pose a substantial public health problem.

EPIDEMIOLOGIC STUDIES OF TUMORS AND CELL PHONE USE: OVERVIEW AND STUDY METHODS

Numerous studies have investigated the relationship between cell phone use and the risk of developing malignant brain tumors (mostly gliomas, which begin in glial cells that surround and support the nerve cells) and tumors of the meninges (meningiomas, which are mostly benign). Several studies have examined cell phone use and risk of tumors of the nerve to the ear (acoustic neuromas, which are benign) /4/. Few studies have examined cell phone use and tumors of the salivary and parotid glands /5, 6/.

Most studies for each of the anatomic sites are case-control studies. These studies identify newly diagnosed cases from hospitals where the cases and diagnosed and treated or from population based cancer registries where cases in a defined geographic region are reported. Persons without the disease, who are from the same population (hospitals or general population) as the cases and are similar in age, sex, race and possibly other features, are selected as controls. The majority of case-control studies obtained questionnaire-derived information about past history of cell phone from cases and controls, and compare history of use in cases to history of use in controls. The case-control study method is frequently used to

study rare conditions so that large numbers of cases can be evaluated /7/. Since 2001, results of individual case-control studies have been reported.

A parallel series of case-control studies, known as the INTERPHONE study, were carried out using a common protocol developed by the International Agency for Research on Cancer. The INTERPHONE studies were carried out in Australia, Canada, Denmark, Finland, France, Germany, Israel, Italy, Japan, New Zealand, Norway, Sweden, and the United Kingdom /8/.

Results from several of the individual studies in INTERPHONE and combined data from a subgroup of five of the studies in northern Europe have been published. Analysis of the combined INTERPHONE datasets is underway, and results will provide more comprehensive and stable risk estimates than results from the individual studies. Much less common than case-control studies are cohort studies in which 'exposed persons' (e.g., cell phone subscribers) are followed up, and incidence of malignant and benign tumors in the exposed group is compared with incidence in an unexposed group or the general population. The cohort study design is not used often for studies of rare diseases because the approach requires followup of very large numbers of persons to obtain stable incidence rate information /7/.

Results of Epidemiologic Studies

Glioma—Two early U.S. case-control studies and a Danish cohort study of cell phone use and glioma found no evidence of a relationship /1/.

More recently, a follow up of 420,000 Danish persons with a first cell phone subscription between 1982 and 1995 through 2002 showed no increase in glioma overall or among 10+ year subscribers /9/. A pooled analysis of five INTERPHONE case-control studies in northern Europe showed a small decrease in glioma risk overall (1,521 cases vs 3,301 controls), and no increase in risks for cumulative years of use, number of calls, cumulative hours of use, years since first use, or use of analog vs. digital phones. Risk was slightly increased for glioma among those with cell phone use on the same side of the head as the tumor /10/.

Meningioma—The Danish cohort study showed no increase of risk of meningioma overall or among 10+ year subscribers among the 420,000 persons followed up through 2002 /9/. The pooled analysis of five INTERPHONE case-control studies in northern Europe showed a small decrease in meningioma risk overall (1,209 cases vs 3,299 controls), and no increase in risks for cumulative years of use, number of calls, cumulative hours of use, years since first use, use of analog vs. digital phones or laterality of tumor relative to laterality of cell phone use /11/.

Acoustic neuroma—The Danish cohort study showed no increase of risk of acoustic neuroma overall or among 10+ year subscribers among the 420,000 persons followed up through 2002/9/. The pooled analysis of five INTERPHONE casecontrol studies in northern Europe showed no significant increase or decrease in risk of acoustic neuromas overall (678 cases vs 3,553 controls), and no increase in risks for cumulative years of use, number of calls, cumulative hours of use, years since first use, or use of analog vs. digital phones. Risk was 80 percent and significantly increased for use of cell phone on the same side of the head as the tumor /12/.

Brain tumor mortality in large occupational cohort studies with radiofrequency exposures—In a follow-up study of 195,775 Motorola workers

employed in manufacturing and testing cell phones during 1976-96 and followed up through 1996, there was no association between radiofrequency exposure and brain tumor mortality /13/. Among 40,581 Navy veterans of the Korean War who were potentially exposed to high-intensity radar, brain tumor mortality was not increased in the entire cohort or in Navy personnel in high exposure occupations /14/.

Trends in brain tumor incidence by age—Assessment of brain tumor incidence trends in the NCI Surveillance Epidemiology and End Results nine long-standing population-based cancer registries showed no change in incidence during 1973-2005 among persons ages 45-64 at diagnosis. For persons diagnosed with brain tumors at ages 0-14 and at ages 15-44, incidence rates increased during 1973-85, but subsequently stabilized.

Incidence rates rose during 1973-90 among persons ages 65 and older before stabilizing thereafter. Initial use of cell phones began around 1992 in the U.S. The incidence trend data provide no evidence that brain tumor incidence has changed in any age group since introduction of cell phones /15/.

FUTURE RESULTS

Forthcoming results from the INTERPHONE combined studies from 13 populations should provide the most stable risk estimates on glioma (based on 2,708 cases), meningioma (2,409 cases), acoustic neuromas and parotid gland tumors (the latter two categories were only studied in some of the individual INTERPHONE study populations).

There is concern about the potentially greater sensitivity of children than adults, but no published epidemiologic studies on cancer risks in relation to cell phone use by children or adolescents. Ongoing case-control studies are investigating the relationship of cell phone use and childhood cancer in Denmark, Norway, Sweden, and Switzerland. Birth cohort studies of 100,000 Danish and the same number of Norwegian children have inquired about cell phone use, and it should be possible to assess cancer risks in these two large cohorts after a few more years.

LIMITATIONS OF EPIDEMIOLOGIC STUDIES

An important limitation of most studies carried out to date is the use of questionnaires to ascertain detailed information about duration, frequency, and cumulative hours of use. The accuracy and completeness of information obtained using questionnaires depends upon the memory of the respondents. In case-control studies, patients with brain tumors may recall cell phone use differently than controls, a problem designated 'recall bias.'

Errors in reporting may differ between cases and controls leading to 'reporting bias.' Participation rates by controls are often substantially lower than participation by cases. Non-participants are likely to differ from participants in socio-demographic characteristics (in many studies persons who participate often have higher levels of education and are more interested in research studies), cell phone use (those who use cell phones infrequently may be less likely to participate), and may differ in other factors. Such differences in participation may result in 'selection bias.' Recall, reporting, and selection bias, which can occur in case-control studies, can be minimized by use of the cohort study design /7/. Other limitations may also affect identification of associations between cell phone use and cancer. The interval between first exposure to a carcinogen and the clinical diagnosis of a tumor may be many years to decades in length.

Hence, insufficient time may have passed between first use and occurrence of brain or other tumors. Results from large numbers of long-term users have not been reported, and the

numbers of long term digital cell phone users are even smaller. Use of 'hands-free' cell phone use, including wireless technology, may account for some variation in exposure but may not have been adequately considered in either case-control or cohort studies.

WHAT CELL PHONE USERS CAN DO TO REDUCE THEIR EXPOSURE TO RADIOFREQUENCY ENERGY

Strategies for reducing exposures to radiofrequency energy from cell phones include making fewer calls, reducing the length of calls, using cell phones only when landline phones are not available, and switching to a type of cell phone with a hands' free device to increase the distance between the antenna and the head of the user.

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