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Review Article

Mobile Phone Radiation : Physiological & Pathophysiologcal Considerations

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Abstract

It is documented that electromagnetic emissions from mobile phones can interfere with brain's signal processing activity due to their oscillatory similitude to the inherent rhythms of the brain, akin to "electromagnetic interference" observed while using mobile phones in aeroplanes.

At high power density levels, thermal effects occur, some of which can be attributed to heat induced stress mechanisms. The less understood non-thermal effects occur at low radio frequency/microwave power density levels and are not accompanied by any body temperature rise. The safety standards set by international agencies are based on thermal effects. For the mobile phones, ICNIRP 1998 guidelines restrict spatial peak of microwave exposure to 2 W/Kg SAR values averaged over 10 g of tissue for 6 minutes.

Some of the reported electromagnetic radiation (EMR) induced adverse effects are brain tumours, male infertility and immune dysfunction with increased susceptibility to infections. Pathophysiological mechanisms of interaction of EMR at plasma membrane are calcium efflux from cell membranes, increased expression of stress proteins, influence on channels/gap junctions in cell membrane, overproduction of reactive oxygen species, ornithine decarboxylase activation, reduction in melatonin levels, decrease in protein kinase C activity, damage to DNA and change in gene expression in brain cells and altered blood- brain barrier.

There are equal number of conflicting reports in literature regarding EMR exposure and brain tumours. A comprehensive review concludes "overall the studies published to date do not demonstrate an increased risk within approximately 10 years of use for any tumour of the brain or any other head tumour." Another review summarises that there is "enough data to convince that long-term exposure to low intensity EMR below the ICNIRP guidelines can promote cancer development". However the time limit for exposure has been suggested as more than 10 years.

For conducting epidemiological studies, some of the difficulties experienced are obtaining unexposed controls or cohorts, follow up of the cohorts, actual dose measurement for exposure assessment in case-control studies, inaccuracy ,recall bias and selective non response in recall of phone use by mobile phone users, long induction times, long latencies (the effects we observe now are of analogue phones that are no longer used) and the rarity of observed malignancies, variable ways of using the phone by the user i.e. left or right ear, head sets/speaker/blue tooth etc. Large-scale epidemiological studies should employ personal MW dosimeters for strict dose measurement and for interpreting actual tissue exposure.

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Introduction

Electromagnetic radiation (EMR) from artificial sources like power distribution networks, cell phones and their base stations, radars, microwave ovens and other sources in daily life exceeds the natural electromagnetic fields by thousand folds. Extensive use of cell phones by public is responsible for "Electropollution" of the environment and has become a matter of health concern.

The International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) issued a press release on May 31, 2011 labelling cell phone radiation as "possibly carcinogenic to humans" and added it to the list to the list of other group 2B agents (1).

Electromagnetic radiation traverses through space at the speed of light and the direction of propagation is perpendicular to time changing electric and magnetic fields. EMR from mobile phones and their base stations is non-ionizing and thus lacks sufficient energy to add or remove electrons from molecules.

As per estimated figures given by Telecom Regulatory Authority of India (TRAI), there are 938 million connections in India as on May 2014, of which 910 million are wireless (2). There are 4.6 billion cell phone users worldwide and India has more than 900 million users (3). Electromagnetic emissions from mobile towers (Base transceiver stations, BTS) emanate at 900 MHz, 1800 MHz, 2100 MHz and 2300 MHz frequencies and from mobile handsets at 900 MHz and 1800 MHz for GSM and at 1800 MHz for CDMA (2). Each BTS has a number of transmitters which feed the antenna placed on the mast. A base station antenna radiates 60 W power and is directional. Power radiated is maximum in primary lobes in the horizontal direction and reduces in the secondary or side lobes near the mast where there is reduced amount of microwave radiation present. Power radiated also decreases with increasing distance from base station as per the inverse square law ($1/R^2$) and increases with the number of channels operating at a particular instant and the number of operators sharing the base station (2).

The cell phones emit 1-2 W of peak radiation. The handset antenna radiates microwave power equally in all directions. Every communication channel has 8 slots. Hence the average power emitted by the handset is 0.125-0.25 W/cm^2 (4).

Radio frequency and microwave radiation (RFR & MWR) are non-ionising with frequencies of electromagnetic spectrum that range from 3 KHz-300 MHz and 300 MHz-300 GHz respectively. In 1980s, the first generation mobile phones of analogue type used sound transmission at 3 KHz - 300 MHz radio frequency range. Since 1991, the second generation mobile phones having digital transmission and GSM technology with data and image transmission capabilities came into vogue. The current third generation phones have fax, e-mail and Internet access (5). The fourth generation of mobile phone technology has faster data transfer than 3G and sophisticated data that requires a lot of bandwidth can be accessed very quickly.

The Microwave safety standards and regulating agencies:

The specific absorption rate (SAR) defines the amount of energy deposited per kilogram of body weight and is a measure for assessing thermal effects. International Commission for Non ionising Radiation Protection (ICNIRP) and the FDA safety standards of USA limit the spatial peak microwave exposure to 2 W/Kg and 1.6 W/Kg SAR values respectively, averaged over 10g of tissue for 6 minutes. Many people in India are not aware of these limits and use mobile phones for long durations (3).

Microwave safety standards implemented by Indian regulating agency:

Department of Telecommunications (DoT) monitors radiation from 10% of the randomly selected base stations (BTS) or as and when, on complaint basis. In 2008, ICNIRP 1998 guidelines for BTS were adopted as Frequency/200 W/Sq. M in 400-2000 MHz range and 10 W/Sq. M in 2-300 GHz range. An Inter-ministerial committee was set up with members from ICMR, DoT, DBT and Ministry of Environment and Forest and in it's meeting on 24/8/2010, the members expressed concern that "Indians are at higher risk

due to tropical climate, low body mass index, low fat content and high environmental EMR". Based on their recommendations, DoT further lowered the safety standards with effect from 1/9/2012 to 1/10 the of ICNIRP guidelines for base stations, i.e. Frequency/2000 W/Sq. M and 1 W/Sq.M at the above mentioned frequencies. For the mobile sets, the new standard is 1.6 W/Kg averaged over 1 gram of tissue, over 6 minutes as compared to earlier ICNIRP standard of 2 W/Kg, averaged over 10 gm tissue, over 6 minutes. These safety standards are stringent as compared to many western countries. Since 1/9/2013 it has become mandatory to display the SAR values on handsets and EMR should be monitored like noise and air pollution through monitoring networks (2).

The microwave safety standards worldwide are set for thermal effects and do not take into account the non thermal effects.

Historical aspects of development of standards:

The initial safety guidelines for radio frequency and microwave radiation (RFR and MWR) were set by American National Standards Institute (ANSI) in 1982 and the US Federal Communications Commission (FCC) on Feb. 26, 1985 based on " thermal effects" (6).

ANSI (1982) published the first exposure standard incorporating 10 fold safety factor for humans exposed to electromagnetic fields between 300 kHz and 100 GHz frequencies. The standard adopted for whole body exposure was 0.4 W/kg averaged over 6 minutes and a 20-fold greater spatial peak SAR exposure over any 1 gram of tissue of 8 W/kg averaged over 6 minutes (7).

Institute of Electrical and Electronic Engineers (IEEE) in 1991 refined this standard and set up a two tier system – one for general public and the other for occupational exposure. The standard for whole body average SAR exposure was set at 0.08 W/kg, averaged over 30 minutes and the spatial peak SAR for any 1 gram of tissue at 1.6 W/kg averaged over 30 minutes for general population. The SAR values were at 0.4 W/Kg for 6 minutes for occupational exposure (7). There were no separate standards set for mobile phones. ANSI in 1992 and FCC in 1996 adopted IEEE1991 standard.

The FCC guidelines in 1996 for cell phone radiation restricted exposure to a maximum SAR of 1.6 watts of energy absorbed per kilogram of body weight per cell phone call that averages 30 minutes when the cell phone is held at the ear (8).

International Commission for Non-Ionizing Radiation Protection (ICNIRP), a non governmental organization followed IEEE 1991 standard in 1998 by adopting the same two-tier system except that both the general public and occupational exposures were averaged over 6 minutes. ICNIRP far field guideline for occupational exposure was set at whole-body average SAR of 0.4 W/kg and maximum spatial peak restriction of SAR was at 10 W/kg. An additional safety factor of 5 was introduced for public exposure, giving an average whole-body SAR limit of 0.08 W/kg and the maximum spatial peak SAR as 2.0 W/kg averaged over 10 gram of tissue (7). This latter restriction is same as for mobile phones.

The Proposed mechanisms of interaction of EMR from cell phones with biological tissues:

Human beings have dual sensitivity i.e. to microwave carrier frequency and the low frequency pulsing at 8.34 Hz of TDMA technology (Time division multiple access, where multiple users can communicate simultaneously with the base station) and 2 Hz of DTX mode (Discontinuous transmission mode, when the user is only listening) that are similar to alpha and delta rhythms of human brain (4). These emissions can interfere with brain's signal processing activity due to their oscillatory similitude to the above inherent rhythms of the brain. This phenomenon is akin to "Electromagnetic interference" (EMI) that occurs while using mobile phones in aeroplanes.

According to US Food and Drug Administration (FDA), EMI from cell phones can disrupt the functioning of pacemakers, especially if the cell phone is placed close to the heart (9). FDA developed a detailed test method to measure this EMI from cell phones on implanted cardiac pacemakers and

defibrillators which became the basis for AAMI standard (Association for the Advancement of Medical Instrumentation). All the manufacturers are to comply with this standard (9).

Two types of effects are described in literature. At high power density levels, with high microwave energy deposition rates, thermal effects are observed. Some of these effects can be explained on the basis of heat induced thermal stress mechanisms. Microwaves have been found to cause cellular heat-stress responses far more easily than other kinds of stress including stress caused by heat (10).

The well documented microwave hearing is perhaps a combination of thermal and non thermal effects ultimately causing a response in the cochlea (10).

The less understood non thermal effects occur at low RF/microwave power density levels and are not accompanied by any body temperature rise.

International agencies concerned with EMR

Some of the International agencies concerned with coordination of research and review on biological effects of RF and MW emissions from mobile phones are Health Evidence Network (HEN) of WHO, International Agency for Research on Cancer (IARC) of WHO, Food and Drug Administration (FDA) of U.S.A, Australian Radiation Protection and Nuclear Safety Agency (ARPANSA), International Commission for Non ionising Radiation Protection (ICNIRP) and National Radiological Protection Board (NRPB) of U.K.

Studies conducted in India: our studies in animals:

Rabbits were exposed 3 hours daily for three months (chronic exposure) at 2.1 GHz, to MWR at 5 mW/cm2 plane wave field near the animal. A control group of rabbits of the same genetic breed were subjected to sham exposures for identical duration in control anechoic chambers, not connected with microwave power source. A comprehensive evaluation of the immunological systems suggested decline in the T lymphocyte counts in peripheral blood, cataract, recurrent infections, weight loss, lymphoid cell depletion in the lymph node, spleen, and appendix and increase in complement receptor positive cells in the popliteal lymph nodes of microwave radiated-SRBC (sheep RBC) immunised rabbits.

Earlier experiments with similar experimental protocol revealed progressive decline in erythrocyte counts, leucocytosis, threefold increase in large lymphocytes, decline in small lymphocyte numbers and neutropenia (11-15).

Pathophysiology of immunological effects & cataract

Chronic microwave radiation leads to immunological derangement and increases susceptibility of animals to infections.

Cataract formation is understood to be due to deformation of glutathione peroxide that protects lens cell proteins and membrane lipids from oxidative damage (16).

Another group of rabbits were subjected to 100 mW/cm^2, for 45 minutes to acute microwave exposures and control group were subjected to heat exposure for identical duration. At high power density levels, acute exposure of rabbits resulted in leucocytosis, lymphopenia, eosinopenia, neutrophilia, decline in T lymphocyte count and enhanced response to mitogen PHA (14, 15).

The observed effects at high power density levels were specific to microwaves as the control group animals exposed to identical heat stress did not reveal these effects.

A recent review by Kesari et al concludes that regular and long term use of microwave devices (mobile phone, microwave oven) at domestic level can have negative impact upon biological systems especially on brain (17). The review highlights role played by reactive oxygen species (ROS) in mediating the effects of microwave radiation. It summarises the work carried out by various scientists in India.

Their work (17) in Wistar rat brain exposed to EMR revealed significant increase in calcium ion efflux and ornithine decarboxylase activity, significant decrease in PKC activity (9.9 GHz/1 W/kg, 2 h/day,

for 35 days), oxidative stress leading to DNA damages in brain (2.45 GHz/0.11 W/Kg, 2 h/day for 35 days), significant increase in apoptotic cells and decrease in protein kinase C activity in hippocampus (900 MHz/ 0.9 W/Kg, 2 h/day for 45 days), reduced melatonin, increased caspase-3 and calcium ion concentration (2.45 GHz/0.14 W/Kg, 2 h/day for 45 days).

Paulraj and Behari reported an increase in single strand DNA breaks in the developing brain cells of rats that were exposed for 35 days to 2.45 and 16.5 GHz fields at 1 and 2.01 W/kg (18).

Gandhi et al reported DNA and chromosomal damage in the form of significant increase in micro nucleated cells in the peripheral blood lymphocytes of individuals using mobile phones (exposed to 800 to 2000 MHz MWR). Correlation between mobile phone use (exposure to MWR) and genetic damage was observed (19).

Several studies confirmed that exposure to electromagnetic fields may increase the incidence of cancer and DNA damage of sperm and brain cells (17- 20).

Chauhan et al reported significantly elevated expression of HSP27, HSP70, OS and UN proteins in Human Lymphoblastoma cell line exposed to EMR, showing stress response (21).

Animal studies / *In vitro* studies conducted in other countries:

The effects of EMR from cell phones on DNA damage have also been reported in various studies from other countries in the last decade (22-25).

Lai and Singh reported an increase in single and double-strand DNA breaks in the brain cells of rats that were exposed for 2 hrs to a 2450 MHz field ,at 0.6-1.2 W/kg. They also found that EMR exposure caused DNA-protein and DNA-DNA cross links and increased apoptosis in biological samples from rats (22, 23).

Lai and Singh demonstrated that treating rats with free radical scavengers blocked the effects of EMR on DNA (24).

A peer-reviewed study reported effects of cell phone radio frequency (RF) radiation on the brain cells of mice and concluded that RF radiation “may damage DNA and change gene expression in brain cells” (25).

Thus one can conclude that EMR enhances free radical activity in cells, which in turn leads to DNA damage (single or double stranded DNA breaks).

A detailed review of neurological and behavioural effects of cell phone radiation is available as a recent update (26). As per this update “almost all the animal studies conducted in mice or rats reported effects”. Recent studies indicated increase in REM sleep in developing rats after chronic exposure and disturbance in REM sleep EEG after long term exposure in the rat (26).

Epidemiological studies:

Careful reviews and meta-analyses of the epidemiological studies (27) supported by well planned long term animal experiments and in vitro studies are the need of the hour to settle controversies in literature. The reviews and meta-analyses worth mentioning are HEN report (5), recent update by Lai (26), results of Interphone study (28-30), review by Ahlbom et al (31), Danish Cohort study (32) and the reports by Hardell group (33-35).

Epidemiological studies reporting no effects:

The Health Evidence Network (HEN) is an information service for public health in the WHO European Region. In it’s report on daily exposure of public to mobile phones it summarises “there is need for further research as no clear cut evidence is available that supports an association between exposure to RF and microwave radiation from mobile phones and direct effects on health”. Until more scientific evidence on mobile phone use is available, it recommends a precautionary approach (5).

The interphone study is a 13 country, 10 year study with identical protocol, coordinated by the International Agency for Research on Cancer (IARC)

WHO. The data on cell phone radiation with endpoint as brain tumour formation were released on May 10th, 2010 (28-30). Most of the studies reported no effects although few suggested increased risk for brain tumours. The results were inconsistent for acoustic neuroma.

Shortcomings

Conclusions were drawn as "overall there was no increase in risk" for glioma or meningioma brain tumours .While these tumours have long induction times of more than 10 years, the average user in the study had less than eight years of cell phone exposure. The studies were conducted with analogue phones in use for more than 10 years.

Anders Ahlbom's team conducted a meta-analysis of existing studies on use of mobile telephones and tumours for ICNIRP. In a comprehensive review authored by the team, they concluded "overall the studies published to date do not demonstrate an increased risk within approximately 10 years of use for any tumour of the brain or any other head tumour" (31).

Shortcomings

The authors pointed out methodological differences between various studies.

The largest study till date, a Danish cohort study of 358, 403 citizens, conducted in October 2011, concluded that "there was no association between tumours of the central nervous system or brain and long term (>10 years) use of mobile phones" (32).

Numerous studies published from 2001-2013 have concluded that there is no association between cell phone use and the development of brain tumours (36-41). In July 2011, a study among children and adolescents found that there was no association between cell phone use and brain tumour risk (42).

Studies finding effects:

The Working Group of 30 scientists from International Agency for Research on Cancer (IARC) at WHO evaluated the carcinogenic effect of radio frequency electromagnetic fields (RF-EMF) from mobile phones and other devices on humans during meetings at Lyon in France (24–31 May 2011) and categorised mobile phones as "Group 2B", i.e. a "possible" human carcinogen. The decision on mobile phones was based mainly on the IARC Interphone study (28-30) and Hardell group of studies from Sweden (33-35).

Hardell et al (33-35) evaluated long-term use of mobile phones and the risk for brain tumours in 16 case-control studies. Consistent pattern of increased risk for acoustic neuroma and glioma with highest risk for ipsilateral exposure of 10 or more years was observed. A meta-analysis of cell phone studies by them in March 2008 revealed a "consistent pattern" between cell phone use and increased risk of developing glioma (33). Similar results were observed by Khurana et al in another study where long term cell phone use of more than 10 years was found to "approximately double the risk" of glioma on the same side of the head where the cell phone was held (43).

A warning to hospital faculty and staff was issued by Director of the University of Pittsburgh Cancer Institute in July 2008, to decrease direct cell phone exposure to the head and body due to a possible connection between cell phone radiation and brain tumours (44).

On Oct. 18, 2012, the Italian Supreme Court ruled that there is a causal relationship between Italian Worker's neuroma tumour and his mobile phone use (occupational use of cell phone, five to six hours a day, over 12 year period) and hence he was entitled to 80% compensation (45).

ARPANSA (Australian Radiation Protection and Nuclear Safety Agency) in 2009 (46) mentions about two Australian reviews on mobile phones and brain tumours .The review by Croft et al agrees with the conclusions made by Ahlbom et al "that the studies do not provide evidence of an association" (47) while Khurana et al (43) suggested "a link between prolonged mobile phone use and the development of an ipsilateral brain tumour".

One of the latest reviews (48) summarises that there is enough data to convince that long-term exposure to low intensity EMR below the official safety limits set up by ICNIRP can promote cancer development. The opinions expressed by the reviewers is supported by reports indicating mortality of US Navy personnel, 20 years after exposure during the Korean War (49) and acceleration of pre-existing cancer development in one year of exposure to microwaves emitted by base transmitting station for mobile communication in Israel (50). In Israel, population living in the area nearby the cell phone base transmitting station (up to 350 M) during one year period revealed 4.15 times more cases of cancer than in the rest of the city. Cancer incidence of women close to base station area was significantly higher as compared with the control area and the whole city. The reviewers also pointed out lacunae in measuring exact microwave exposure in epidemiological research and suggested German studies employing personal microwave dosimeters as an example (51).

Other studies published from 2005-2013 have similarly concluded that there is an association between cell phone use and increased risk of developing brain and head tumours (52-54). There is no substantial risk of acoustic neuroma in the first decade after starting mobile phone use but an increase in risk after longer term use or after a longer lag period could not be ruled out with odds ratio at 1.8 after 10 years of use (52). There were suggestions of an increased risk of glioma in long-term mobile phone users with high radio frequency exposure and apparently much smaller increases in meningioma risk. The authors concluded that "uncertainty of these results requires that they be replicated before a causal interpretation can be made" (53).

Postulated pathophysiological mechanisms for carcinogenesis:

Brain is one of the most studied organs for elucidating effects of electromagnetic radiation from cell phones. Mobile phones when held close to the ear result in comparably high levels of microwave exposure in the near field with maximum deposition of energy in the head of the user.

A number of pathophysiological mechanisms acting at plasma membrane have been postulated. Plasma membrane is suggested as the target at cellular level.

Mobile phone radiation can affect channels in the cell membrane by inhibiting or closing the gap junctions leading to malignancies of the brain such as glioma, meningioma, acoustic neuroma and salivary gland tumours (16, 27, 31, 55).

A review by Desai et al summarises possible pathophysiological mechanisms (56).

NADH oxidase enzyme is identified as one of the target enzymes of EMR interaction at plasma membrane with production of Reactive Oxygen Species (ROS) leading to activation of matrix metalloproteinases, release of epidermal growth factor, activation of extracellular signal regulated kinases (ERKs), induction of stress kinases, activation of MAP (mitogen activated protein) kinase, stimulation of phosphorylation of heat shock proteins and inhibition of apoptosis pathway in a sequential cascade. With inhibition of apoptosis damaged DNA (single strand and double strand breaks and micronuclei formation) accumulates in the cell and causes uncontrolled cell proliferation (56).

On the other hand stimulation of apoptosis with significant increase in Annexin V after exposure to EMR (based on the capability of cells to repair DNA) has also been reported. Increases in ROS production can trigger over expression of ODC and decline in PKC activity, both of which are linked to progression of cancer. Changes in intracellular calcium levels and activities of ODC and PKC are interrelated. Accumulation of free radicals affects various cellular and physiological processes like gene expression, release of calcium from intracellular storage sites and cell growth. Increase in ROS production or decrease in antioxidant activity have independently been reported to be responsible for the observed effects (56).

Rao et al studied the effects of non thermal EMR on calcium dynamics in stem cell derived neuronal cells and discovered a significant increase in intracellular calcium spikes (57).

Pathophysiological mechanisms in children

In a Danish National cohort study, mothers of 13,159 children filled up a follow-up questionnaire reporting their use of cell phones during pregnancy as well as by the child when the children reached 7 years age. Behavioural, emotional and hyperactivity problems were reported in these children with odds ratios at 1.8 (58). These findings were replicated later by another study by the same authors (59). On December 12, 2012, the American Academy of Pediatrics sent a letter to the U.S. Federal Communications Commission (FCC) requesting reassessment of cell phone exposure limits (60).

Pathophysiological effects on various physiological systems

The SAR values depend upon geometry and structure of the skull and are much higher for child head (48). The differences in bone density and the amount of fluid in a child's brain compared to an adult's brain could allow children to absorb greater quantities of RF (radio frequency) energy deeper into their brains than adults (60).

Electromagnetic Hypersensitivity is reported in many individuals who are sensitive to cellphone radiation and other forms of radio frequency energy. Various allergic symptoms like ringing in the ears, headaches, dizziness, irregular heartbeat, memory and sleep problems are experienced (60).

Increased glucose metabolism indicating increased metabolic activity in the areas of the brain closest to the cell phone antenna were observed by some authors as a biological non thermal effect of cell phone radiation (61). Further studies are needed to assess if these effects could have potential long-term harmful consequences (61).

Pathophysiology of decreased male fertility

Review of the existing literature exploring the effects of radio frequency electromagnetic radiation (RF-EMR) on the male reproductive function in experimental animals and humans indicated decreases in sperm count and motility (56). In men using mobile phones decreased sperm concentration, decreased motility and decreased viability and morphology directly related to the duration of mobile phone use were reported (62-63) which might contribute to male infertility.

Oxidative stress and ROS formation have been reported. Decline in sperm motility has been attributed to decline in PKC enzyme activity due to exposure to cell phone EMR (56).

Pathophysiology of effects on CVS

According to the results of a study, mobile phones can affect the heart rate, TP segment and time of T wave. One study has shown significant difference between heart rate during talking in comparison with heart rate during ringing and resting in both genders (64).

Pathophysiology of nervous system

An update of reports on neurological effects of non-ionizing electromagnetic fields published in literature between 2007-2014 by Henry Lai (26) suggests neurological effects in 68% publications and absence of effects in 32% publications. The neurological effects described in the review (26) are changes in brain electrical activities after acute exposure to cell phone radiation like – event related potentials, changes of the alpha-wave power of EEG after exposure to 2G but not 3 G, increased slow-wave activity in humans during exposure to pulse-modulated RFR toward the end of the sleep period and RFR interaction with brain epileptic foci in epileptic patients. Similar EEG effects with both 2G and 3G radiations were found by others. However, some authors reported no significant effects on resting EEG and event-related potentials in humans after exposure to cell phone EMR. The review mentions both significant and non significant effects in sleep EEG and mobile phone-like emissions affecting the EEG during non-REM sleep.

The difficulties and controversies:

Due to extensive use of mobile phones, obtaining unexposed controls or cohorts for conducting epidemiological studies is difficult. One of the key methodological problem in conducting case-control

studies is actual dose measurement for exposure assessment which is often based on recall of mobile phone use by the user. This introduces inaccuracy, recall bias and selective non response in recall of mobile phone use. Long induction times, long latencies and the rarity of observed malignancies, follow up of the cohorts, variable ways of using the phone by the user - i.e. left or right ear, head sets/ speaker/blue tooth etc. further complicate interpretations (27). Finally, the transmission output of telephones is constantly changing, waxing and waning as it adjusts to the distance from cell towers (the distance from cell towers changes as a person moves from location to location) or to shielding materials such as building walls (27).

For the animal experiments too there are difficulties in quantifying exposure parameters like intensity of exposure, scaling of the absorption and internal field distribution pattern between animals and humans.

Future goals for research:

Large scale experiments with studies conducted in vitro, by exposing various cell lines/tissue cultures/ blood cells to EMR, supported by animal studies with identical exposure parameters will help in arriving at logical conclusions. Dosimetry is also important for in vitro and in vivo animal studies for quantifying the intensity of exposure and absorption and internal field distribution of EMR in order to extrapolate the results to humans.

For the epidemiological studies, follow up of cohorts for long durations (beyond 10 years) will help in identifying potential cancer risk. Large-scale epidemiological studies should employ personal MW dosimeters for strict dose measurement and for interpreting actual tissue exposure (48). Without metering, a person's actual tissue exposure to EMR cannot be appropriately estimated, even with the help of telephone call records.

Database registries/repositories should be maintained by various scientists/scientific bodies and made available online for easy referral and replication and reproducibility of results.

The official recommendations by ICNIRP and other international standards must be revised.

Recommendations:

Preventive measures like use of head sets or blue tooth or using the cell phone in speaker mode, reduction in length and number of calls should be advocated. Holding a cell phone away from the body while using a wired earpiece or speaker phone (also not placing the cell phone in the front pocket while it is switched on) lowers the amount of radiation absorbed, and text messaging, rather than talking, further lowers that amount. Cell phone use should be minimised in children, adolescents and pregnant women as a child's brain absorbs twice as much radiation as an adult brain. Cell phones should not be used when the signal is weak like in a moving vehicle or in a lift as the phone increases its signal strength to compensate (61).

One cannot ignore the beneficial effects of mobile phones in cases of emergency as many lives are saved. Till then prudent avoidance is advocated.

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