Discussion/Action Item 1i CEAC April 7, 2011

## **Research on the Effects of Cell Phone Radiation on Human Sperm**

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## Summary

The following terms were used in a PubMed search: (cell or mobile) phone sperm. Fourteen English-language, papers were found that examined the effects of cell phone radiation on human sperm including nine original studies and five review papers.

Eight of the nine original studies reported adverse effects of cell phone radiation on at least one of four outcomes: sperm count (C), motility (M), viability (V) or morphology (S). The adverse effects obtained in these studies were as follows: C/M/V/S (Agarwal et al., 2008a); M/V (Agarwal et al., 2009; De Iuliis et al., 2009); M/S (Wdowiak et al, 2007); M (Erogul et al, 2006; Fejes et al., 2005); and S (Falzone et al., 2008; Falzone et al., 2011). The ninth study examined sperm for signs of pre-apoptosis but found no evidence for this mechanism (Falzone et al., 2010). Cell phone radiation was associated with decreased sperm motility (M) in six of the eight studies that assessed this outcome. The next most commonly observed effect was reduced viability (V) in three studies. Note that not all studies measured each of these four outcomes.

The research abstracts from the search follow. The original studies are in the first section followed by the review papers. The abstracts are listed in alphabetical order by first author.

# **Original Research Studies**

Agarwal A, Deepinder F, Sharma RK, Ranga G, Li J. (2008a). Effect of cell phone usage on semen analysis in men attending infertility clinic: an observational study. Fertil Steril. 2008 Jan; 89(1):124-8. Epub 2007 May 4.

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## Abstract

OBJECTIVE: To investigate the effect of cell phone use on various markers of semen quality.

DESIGN: Observational study.

SETTING: Infertility clinic.

PATIENT(S): Three hundred sixty-one men undergoing infertility evaluation were divided into four groups according to their active cell phone use: group A: no use; group B: <2 h/day; group C: 2-4 h/day; and group D: >4 h/day.

INTERVENTION(S): None.

MAIN OUTCOME MEASURE(S): Sperm parameters (volume, liquefaction time, pH, viscosity, sperm count, motility, viability, and morphology).

RESULT(S): The comparisons of mean sperm count, motility, viability, and normal morphology among four different cell phone user groups were statistically significant. Mean sperm motility, viability, and normal morphology were significantly different in cell phone user groups within two sperm count groups. The laboratory values of the above four sperm parameters decreased in all four cell phone user groups as the duration of daily exposure to cell phones increased.

CONCLUSION(S): Use of cell phones decrease the semen quality in men by decreasing the sperm count, motility, viability, and normal morphology. The decrease in sperm parameters was dependent on the duration of daily exposure to cell phones and independent of the initial semen quality.

## PMID: 17482179

Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, Sharma R. (2009). Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril. 2009 Oct;92(4):1318-25. Epub 2008 Sep 20.

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#### Abstract

OBJECTIVE: To evaluate effects of cellular phone radiofrequency electromagnetic waves (RF-EMW) during talk mode on unprocessed (neat) ejaculated human semen.

DESIGN: Prospective pilot study.

SETTING: Center for reproductive medicine laboratory in tertiary hospital setting.

SAMPLES: Neat semen samples from normal healthy donors (n = 23) and infertile patients (n = 9).

INTERVENTION(S): After liquefaction, neat semen samples were divided into two aliquots. One aliquot (experimental) from each patient was exposed to cellular phone radiation (in talk mode) for 1 h, and the second aliquot (unexposed) served as the control sample under identical conditions.

MAIN OUTCOME MEASURE(S): Evaluation of sperm parameters (motility, viability), reactive oxygen species (ROS), total antioxidant capacity (TAC) of semen, ROS-TAC score, and sperm DNA damage.

RESULT(S): Samples exposed to RF-EMW showed a significant decrease in sperm motility and viability, increase in ROS level, and decrease in ROS-TAC score. Levels of TAC and DNA damage showed no significant differences from the unexposed group.

CONCLUSION(S): Radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility.

## PMID: 18804757

De Iuliis GN, Newey RJ, King BV, Aitken RJ. Mobile phone radiation induces reactive oxygen species production and DNA damage in human spermatozoa in vitro. PLoS One. 2009 Jul 31;4(7):e6446.

ARC Centre of Excellence in Biotechnology and Development, Callaghan, New South Wales, Australia.

## Abstract

BACKGROUND: In recent times there has been some controversy over the impact of electromagnetic radiation on human health. The significance of mobile phone radiation on male reproduction is a key element of this debate since several studies have suggested a relationship between mobile phone use and semen quality. The potential mechanisms involved have not been established, however, human spermatozoa are known to be particularly vulnerable to oxidative stress by virtue of the abundant availability of substrates for free radical attack and the lack of cytoplasmic space to accommodate antioxidant enzymes. Moreover, the induction of oxidative stress in these cells not only perturbs their capacity for fertilization but also contributes to sperm DNA damage. The latter has, in turn, been linked with poor fertility, an increased incidence of miscarriage and morbidity in the offspring, including childhood cancer. In light of these associations, we have analyzed the influence of RF-EMR on the cell biology of human spermatozoa in vitro.

PRINCIPAL FINDINGS: Purified human spermatozoa were exposed to radio-frequency electromagnetic radiation (RF-EMR) tuned to 1.8 GHz and covering a range of specific absorption rates (SAR) from 0.4 W/kg to 27.5 W/kg. In step with increasing SAR, motility and vitality were significantly reduced after RF-EMR exposure, while the mitochondrial generation of reactive oxygen species and DNA

fragmentation were significantly elevated (P<0.001). Furthermore, we also observed highly significant relationships between SAR, the oxidative DNA damage bio-marker, 8-OH-dG, and DNA fragmentation after RF-EMR exposure.

CONCLUSIONS: RF-EMR in both the power density and frequency range of mobile phones enhances mitochondrial reactive oxygen species generation by human spermatozoa, decreasing the motility and vitality of these cells while stimulating DNA base adduct formation and, ultimately DNA fragmentation. These findings have clear implications for the safety of extensive mobile phone use by males of reproductive age, potentially affecting both their fertility and the health and wellbeing of their offspring.

## PMID: 19649291

Erogul O, Oztas E, Yildirim I, Kir T, Aydur E, Komesli G, Irkilata HC, Irmak MK, Peker AF. Effects of electromagnetic radiation from a cellular phone on human sperm motility: an in vitro study. Arch Med Res. 2006 Oct;37(7):840-3.

Biomedical and Clinical Engineering Centre, Gulhane Military Medical Academy, Etlik, Ankara, Turkey.

## Abstract

BACKGROUND: There has been growing public concern on the effects of electromagnetic radiation (EMR) emitted by cellular phones on human health. Many studies have recently been published on this topic. However, possible consequences of the cellular phone usage on human sperm parameters have not been investigated adequately.

METHODS: A total number of 27 males were enrolled in the study. The semen sample obtained from each participant was divided equally into two parts. One of the specimens was exposed to EMR emitted by an activated 900 MHz cellular phone, whereas the other was not. The concentration and motility of the specimens were compared to analyze the effects of EMR. Assessment of sperm movement in all specimens was performed using four criteria: (A) rapid progressive, (B) slow progressive, (C) nonprogressive, (D) no motility.

RESULTS: Statistically significant changes were observed in the rapid progressive, slow progressive and no-motility categories of sperm movement. EMR exposure caused a subtle decrease in the rapid progressive and slow progressive sperm movement. It also caused an increase in the no-motility category of sperm movement. There was no statistically significant difference in the sperm concentration between two groups.

CONCLUSIONS: These data suggest that EMR emitted by cellular phone influences human sperm motility. In addition to these acute adverse effects of EMR on sperm motility, long-term EMR exposure may lead to behavioral or structural changes of the male germ cell. These effects may be observed later in life, and they are to be investigated more seriously.

Falzone N, Huyser C, Becker P, Leszczynski D, Franken DR. The effect of pulsed 900-MHz GSM mobile phone radiation on the acrosome reaction, head morphometry and zona binding of human spermatozoa. Int J Androl. 2011 Feb;34(1):20-6. doi: 10.1111/j.1365-2605.2010.01054.x.

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# Abstract

Several recent studies have indicated that radiofrequency electromagnetic fields (RF-EMF) have an adverse effect on human sperm quality, which could translate into an effect on fertilization potential. This study evaluated the effect of RF-EMF on sperm-specific characteristics to assess the fertilizing competence of sperm. Highly motile human spermatozoa were exposed for 1 h to 900-MHz mobile phone radiation at a specific absorption rate of 2.0 W/kg and examined at various times after exposure. The acrosome reaction was evaluated using flow cytometry. The radiation did not affect sperm propensity for the acrosome reaction. Morphometric parameters were assessed using computer-assisted sperm analysis. Significant reduction in sperm head area ( $9.2 \pm 0.7 \ \mu m^2 \ vs.$  18.8  $\pm 1.4 \ \mu m^2$ ) and acrosome percentage of the head area ( $21.5 \pm 4\% \ vs.$   $35.5 \pm 11.4\%$ ) was reported among exposed sperm compared with unexposed controls. Sperm-zona binding was assessed directly after exposure using the hemizona assay. The mean number of zona-bound sperm of the test hemizona and controls was  $22.8 \pm 12.4$  and  $31.8 \pm 12.8 \ (p < 0.05)$ , respectively. This study concludes that although RF-EMF exposure did not adversely affect the acrosome reaction, it had a significant effect on sperm morphometry. In addition, a significant decrease in sperm binding to the hemizona was observed. These results could indicate a significant effect of RF-EMF on sperm fertilization potential.

PMID: 20236367

Falzone N, Huyser C, Franken DR, Leszczynski D. Mobile phone radiation does not induce pro-apoptosis effects in human spermatozoa. Radiat Res. 2010 Aug;174(2):169-76.

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## Abstract

Recent reports suggest that mobile phone radiation may diminish male fertility. However, the effects of this radiation on human spermatozoa are largely unknown. The present study examined effects of the radiation on induction of apoptosis-related properties in human spermatozoa. Ejaculated, density-purified, highly motile human spermatozoa were exposed to mobile phone radiation at specific absorption rates (SARs) of 2.0 and 5.7 W/kg. At various times after exposure, flow cytometry was used to examine caspase 3 activity, externalization of phosphatidylserine (PS), induction of DNA strand breaks, and generation of reactive oxygen species. Mobile phone radiation had no statistically significant effect on any of the parameters studied. This suggests that the impairment of fertility reported in some studies was not caused by the induction of apoptosis in spermatozoa.

Falzone N, Huyser C, Fourie F, Toivo T, Leszczynski D, Franken D. In vitro effect of pulsed 900 MHz GSM radiation on mitochondrial membrane potential and motility of human spermatozoa. Bioelectromagnetics. 2008 May;29(4):268-76.

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## Abstract

Ejaculated, density purified, human spermatozoa were exposed to pulsed 900 MHz GSM mobile phone radiation at two specific absorption rate levels (SAR 2.0 and 5.7 W/kg) and compared with controls over time. Change in sperm mitochondrial membrane potential was analysed using flow cytometry. Sperm motility was determined by computer assisted sperm analysis (CASA). There was no effect of pulsed 900 MHz GSM radiation on mitochondrial membrane potential. This was also the case for all kinematic parameters assessed at a SAR of 2.0 W/kg. However, over time, the two kinematic parameters straight line velocity (VSL) and beat-cross frequency (BCF) were significantly impaired (P < 0.05) after the exposure at SAR 5.7 W/kg and no exposure by time interaction was present. This result should not be ascribed to thermal effects, due to the cooling methods employed in the RF chamber and temperature control within the incubator.

## PMID: 18163440

Fejes I, Závaczki Z, Szöllosi J, Koloszár S, Daru J, Kovács L, Pál A. Is there a relationship between cell phone use and semen quality? Arch Androl. 2005 Sep-Oct;51(5):385-93.

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## Abstract

This study was conducted to determine a possible relationship between regular cell phone use and different human semen attributes. The history-taking of men in our university clinic was supplemented with questions concerning cell phone use habits, including possession, daily standby position and daily transmission times. Semen analyses were performed by conventional methods. Statistics were calculated with SPSS statistical software. A total of 371 were included in the study. The duration of possession and the daily transmission time correlated negatively with the proportion of rapid progressive motile sperm (r = -0.12 and r = -0.19, respectively), and positively with the proportion of slow progressive motile sperm (r = 0.12 and r = 0.28, respectively). The low and high transmitter groups also differed in the proportion of rapid progressive motile sperm (48.7% vs. 40.6%). The prolonged use of cell phones may have negative effects on the sperm motility characteristics.

Wdowiak A, Wdowiak L, Wiktor H. Evaluation of the effect of using mobile phones on male fertility. Ann Agric Environ Med. 2007;14(1):169-72.

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# Abstract

The problem of the lack of offspring is a phenomenon concerning approximately 15% of married couples in Poland. Infertility is defined as inability to conceive after a year of sexual intercourses without the use of contraceptives. In half of the cases the causative factor is the male. Males are exposed to the effect of various environmental factors, which may decrease their reproductive capabilities. A decrease in male fertility is a phenomenon which occurs within years, which may suggest that one of the reasons for the decrease in semen parameters is the effect of the development of techniques in the surrounding environment. A hazardous effect on male fertility may be manifested by a decrease in the amount of sperm cells, disorders in their mobility, as well as structure. The causative agents may be chemical substances, ionizing radiation, stress, as well as electromagnetic waves. The objective of the study was the determination of the effect of the usage of cellular phones on the fertility of males subjected to marital infertility therapy. The following groups were selected from among 304 males covered by the study: Group A: 99 patients who did not use mobile phones, Group B: 157 males who have used GSM equipment sporadically for the period of 1-2 years, and Group C: 48 people who have been regularly using mobile phone for more than 2 years. In the analysis of the effect of GSM equipment on the semen it was noted that an increase in the percentage of sperm cells of abnormal morphology is associated with the duration of exposure to the waves emitted by the GSM phone. It was also confirmed that a decrease in the percentage of sperm cells in vital progressing motility in the semen is correlated with the frequency of using mobile phones.

## **Review Papers**

Agarwal A, Desai NR, Ruffoli R, Carpi A. (2008b). Lifestyle and testicular dysfunction: a brief update. Biomed Pharmacother. Oct;62(8):550-3. Epub 2008b Aug 8.

Center for Reproductive Medicine, Glickman Urological and Kidney Institute and Obst/Gyne and Women's Health Institute, Cleveland Clinic, Cleveland, OH, USA. agarwaa@ccf.org

#### Abstract

The incidence of testicular cancer, cryptorchidism and defective spermatogenesis is increasing probably due to environmental and lifestyle-related factors. The aim of this review is to briefly describe and comment on the principal lifestyle factors. The recent findings that the electromagnetic waves following the use of the cell phone and the prolonged exposure to the noise stress cause relevant testicular dysfunction in man or animals reinforce the hypothesis of the importance of lifestyle-related factors.

#### PMID: 18771892

Deepinder F, Makker K, Agarwal A. Cell phones and male infertility: dissecting the relationship. Reprod Biomed Online. 2007 Sep;15(3):266-70.

Reproductive Research Center, Glickman Urological and Kidney Institute and Department of Obstetrics-Gynecology, Cleveland Clinic, 9500 Euclid Avenue, Desk A19.1, Cleveland, Ohio 44195, USA.

#### Abstract

There has been a tremendous increase in the use of mobile phones in the past decade and concerns are growing about the possible hazardous effects of radio-frequency electromagnetic waves (EMW) emitted by these devices on human health. Preliminary studies, though with limitations in study design, suggest a possible link between cell phone use and infertility. A recent study found that use of cell phones adversely affects the quality of semen by decreasing the sperm counts, motility, viability and morphology. Evidence of detrimental effect of mobile phones on male fertility is still equivocal as studies have revealed a wide spectrum of possible effects ranging from insignificant effects to variable degrees of testicular damage. Although previous studies suggested a role of cell phone use in male infertility, the mode of action of EMW emitted from cell phones on the male reproductive system is still unclear. EMW can affect the reproductive system via an EMW-specific effect, thermal molecular effect or combination of both. Studies performed on human males are scarce and therefore further studies with a careful design are needed to determine the effect of cell phone use on male-fertilizing potential.

Derias EM, Stefanis P, Drakeley A, Gazvani R, Lewis-Jones DI. Growing concern over the safety of using mobile phones and male fertility. Arch Androl. 2006 Jan-Feb;52(1):9-14.

Hewitt Centre for Reproductive Medicine, Liverpool Women's Hospital, Liverpool, UK.

## Abstract

There are growing concerns about the possible hazards of electromagnetic waves emitted by mobile phones on human health. One of the biggest concerns is their possible association with increased risk of cancer and their possible effects on cellular DNA. Electromagnetic waves can inflict their results through both thermal and non-thermal effects. There are many animal studies that show that electromagnetic waves have a wide range of damaging effects on the male reproductive system and sperm parameters. However, similar studies are quite limited in humans, and the results of animal studies should be interpreted with caution when considering their application to humans. Large controlled studies are required before confirming such possible effects on male fertility.

PMID: 16338863

Desai NR, Kesari KK, Agarwal A. Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system. Reprod Biol Endocrinol. 2009 Oct 22;7:114.

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## Abstract

Hazardous health effects stemming from exposure to radiofrequency electromagnetic waves (RF-EMW) emitted from cell phones have been reported in the literature. However, the cellular target of RF-EMW is still controversial. This review identifies the plasma membrane as a target of RF-EMW. In addition, the effects of RF-EMW on plasma membrane structures (i.e. NADH oxidase, phosphatidylserine, ornithine decarboxylase) and voltage-gated calcium channels are discussed. We explore the disturbance in reactive oxygen species (ROS) metabolism caused by RF-EMW and delineate NADH oxidase mediated ROS formation as playing a central role in oxidative stress (OS) due to cell phone radiation (with a focus on the male reproductive system). This review also addresses: 1) the controversial effects of RF-EMW on mammalian cells and sperm DNA as well as its effect on apoptosis, 2) epidemiological, in vivo animal and in vitro studies on the effect of RF-EMW on male reproductive system, and 3) finally, exposure assessment and dosimetry by computational biomodeling.

Makker K, Varghese A, Desai NR, Mouradi R, Agarwal A. Cell phones: modern man's nemesis? Reprod Biomed Online. 2009 Jan;18(1):148-57.

Center for Reproductive Medicine, Cleveland Clinic, Cleveland, Ohio, USA.

## Abstract

Over the past decade, the use of mobile phones has increased significantly. However, with every technological development comes some element of health concern, and cell phones are no exception. Recently, various studies have highlighted the negative effects of cell phone exposure on human health, and concerns about possible hazards related to cell phone exposure have been growing. This is a comprehensive, up-to-the-minute overview of the effects of cell phone exposure on human health. The types of cell phones and cell phone technologies currently used in the world are discussed in an attempt to improve the understanding of the technical aspects, including the effect of cell phone exposure on the cardiovascular system, sleep and cognitive function, as well as localized and general adverse effects, genotoxicity potential, neurohormonal secretion and tumour induction. The proposed mechanisms by which cell phones adversely affect various aspects of human health, and male fertility in particular, are explained, and the emerging molecular techniques and approaches for elucidating the effects of mobile phone radiation on cellular physiology using high-throughput screening techniques, such as metabolomics and microarrays, are discussed. A novel study is described, which is looking at changes in semen parameters, oxidative stress markers and sperm DNA damage in semen samples exposed in vitro to cell phone radiation.