January 24, 2024

Static/ELF-EMF reproduction

(E)= effect; (NE)= no effect

AE= acute exposure; BE= behavioral effect; CE= long-term/repeated exposure; DE= developmental study; F= female reproduction component, e.g., ovary; FC= functional change including fertility; GE= genetic effect (DNA damage/gene expression); HU= human study (including tissues from humans); IU= in utero/in ovo exposure; IV= in vitro; IX= interaction with other entity; M= male reproduction component, e.g., testis; ME= morphological/cellular effect; MO= molecular/hormonal effect; NU= neurological effect, including electrophysiology; OX= oxidative effect; PN= post-natal exposure; VO= in vivo

E= 65 (74%) NE= 22 (26%)

(E)

Ahmadi SS, Khaki AA, Ainehchi N, Alihemmati A, Khatooni AA, Khaki A, Asghari A. Effect of non-ionizing electromagnetic field on the alteration of ovarian follicles in rats. Electron Physician 8(3):2168-2174, 2016. (CE, F, IU, ME, VO)

Introduction: In recent years, there has been an increase in the attention paid to safety effects, environmental and society's health, extremely low frequency electromagnetic fields (ELF-EMF), and radio frequency electromagnetic fields (RF-EMF). The aim of this research was to determine the effect of EMF on the alteration of ovarian follicles. Methods: In this experimental study at Tabriz Medical University in 2015, we did EMF exposures and assessed the alteration of rats' ovarian follicles. Thirty three-month old rats were selected randomly from laboratory animals, and, after their ages and weights were determined, they were divided randomly into three groups. The control group consisted of 10 rats without any treatment, and they were kept in normal conditions. The second group of rats was influenced by a magnetic field of 50 Hz for eight weeks (three weeks intrauterine and five weeks ectopic). The third group of rats was influenced by a magnetic field of 50 Hz for 13 weeks (three weeks intrauterine and ten weeks ectopic). Samples were fixed in 10% buffered formaldehyde and cleared with Xylol and embedded in paraffin. After sectioning and staining, samples were studied by optic microscopy. Finally, SPSS version 17, were used for data analysis. Results: EMF radiation increased the harmful effects on the formation of ovarian follicles and oocytes implantation. Studies on the effects of electromagnetic fields on ovarian follicles have shown that the nuclei of the oocytes become smaller and change shape. There were significant, harmful changes in the groups affected by electromagnetic waves. Atresia of ovarian follicles was significantly significant in both study groups compared to the control group (p < 0.05). Conclusion: Exposure to electromagnetic fields during embryonic development can cause morphological changes in oocytes and affect the differentiation of oocytes and folliculogenesis, resulting in decreased ovarian reserve leading to infertility or reduced fertility.

(NE)Akdag MZ, Dasdag S, Aksen F, Isik B, Yilmaz F. Effect of ELF magnetic fields on lipid peroxidation, sperm count, p53, and trace elements. Med Sci Monit. 12(11):BR366-371, 2006. (CE, M, ME, OX, VO)

BACKGROUND: Some epidemiological and laboratory studies suggest a possible connection between extremely low-frequency (ELF) magnetic fields and certain illnesses, such as cancer, immune suppression, as well as reproductive toxic effects and abnormalities. Therefore, the aim of this study was to investigate the effects of ELF magnetic fields (1.35 mT) on sperm count, malondialdehyde concentration, the histology of such organs as the testes, brain, liver, and kidney tissues, p53 immunoreactivity of bone marrow, and the serum concentrations of Cu2+, Zn2+, Mn2+, and Fe3+ in rats. MATERIAL/METHODS: Sixteen Sprague-Dawley male rats were divided into two groups. The rats in the experimental group were exposed to an ELF magnetic field 2 hr/day for 2 months (7 days a week). The rats in the control group were not exposed to the ELF magnetic field. The exposure was performed in a Faraday cage (130 x 65 x 80 cm) with grounded shielding against the electric component. The Mann-Whitney U-test was used for the statistical analysis of the data. RESULTS: Magnetic field measurements showed that, under the experimental conditions, the magnetic field-exposure system produced a stable flux density of 1.35+/-0.018 mT and a stable frequency of 50 Hz, with negligible harmonics and no transients. However, no statistically significant alteration was observed in the parameters measured in this study except in Mn2+ concentrations (p<0.001). CONCLUSIONS: The present study found no evidence of an adverse effect of ELF magnetic fields on the measured parameters except for significantly increased Mn2+ concentrations (p<0.001).

(E)Al-Akhras MA, Darmani H, Elbetieha A. Influence of 50 Hz magnetic field on sex hormones and other fertility parameters of adult male rats. Bioelectromagnetics. 27(2):127-131, 2006. (CE, M, ME, MO, VO)

The effects of an extremely low frequency (ELF) magnetic field on the sex hormones and other fertility parameters of adult male Sprague-Dawley rats were investigated. Adult male rats were exposed to a 50 Hz sinusoidal magnetic field at approximately 25 microT (rms) for 18 consecutive weeks. There were no significant effects on the absolute body weight and the weight of the testes of the exposed rats. However, the weights of seminal vesicles and preputial glands were significantly reduced in the exposed male rats. Similarly, a significant effects on the serum levels of male follicle stimulating hormone (FSH) during the 18 weeks of exposure period. On the other hand, there was a significant increase in the serum levels of male luteinizing hormone (LH) after 18 weeks of exposure (P < .005), while testosterone levels were significantly decreased only after 6 and 12 weeks of the exposure period. These results suggest that long term exposure to ELF could have adverse effects on mammalian fertility and reproduction.

(E)Al-Akhras M. Influence of 50 Hz magnetic field on sex hormones and body, uterine, and ovarian weights of adult female rats. Electromagn Biol Med 27(2):155-163, 2008. (CE, F, ME, MO, VO)

The effects of extremely low-frequency (ELF) magnetic fields on sex hormones of adult female Spague-Dawley rats were investigated. Adult female rats were exposed to a 50 Hz sinusoidal magnetic field at approximately 25 microT (rms) for 18 weeks before they returned to their normal life with unexposed counterparts. Serum level of Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), progesterone, and estrogen were measured before, after, and during the exposure. Body and uterine weights were not affected by the field. A significant reduction in absolute and relative ovarian weights in exposed rats was observed when compared with shamexposed controls (P < 0.05). The reduction in the levels of gonadotropins (FSH and LH) was significant after six weeks of exposure (P < 0.005). FSH levels were affected only on week 6 of exposure while LH remained affected during at 12 and 18 weeks (P < 0.05). Interestingly, no significant effects were found at 6 and 12 weeks after removing the field. The level of progesterone and estrogen was significantly decreased after 12 weeks of exposure (P < 0.05), while no other effects on progesterone level was observed during exposure or after removing the exposure. The level of estrogen was also significantly reduced at 12 weeks after removing the field (P < 0.05). These results suggest possible adverse effect on mammalian fertility and reproduction. The effects of ELF-MF on sex hormones were shown to be partly reversible.

(E)Amara S, Abdelmelek H, Garrel C, Guiraud P, Douki T, Ravanat JL, Favier A, Sakly M, Ben Rhouma K. Effects of subchronic exposure to static magnetic field on testicular function in rats. Arch Med Res. 37(8):947-952, 2006. (CE, GE, M, MO, OX, VO)

BACKGROUND: The aim of this study was to investigate the effect of static magnetic field (SMF) exposure on testicular function, antioxidant status and DNA oxidation in rats. METHODS: Male adult rats were exposed to SMF (128 mT; 1 h/day for 30 days). After sacrifice, the epididymal sperm number was counted. Testosterone concentration in plasma and testis was measured by radioimmunoassay. MDA level and GPx, CAT and SOD activities were used as markers of oxidative stress in testis. The 8-oxo-dG level is measured by the HPLC-EC system. RESULTS: Subchronic exposure to SMF has no effect on epididymal sperm count, spermatozoa motility and genital organ weight. In contrast, SMF induces a decrease of testicular and plasmatic testosterone levels, respectively $(1.48 \pm 0.56 \text{ vs}, 4.66 \pm 0.51 \text{ ng/g}, \text{p} \le 0.05; 0.97 \text{ s})$ +/-0.16 vs. 1.64 +/-0.18 ng/mL, p<0.05). Exposed rats displayed an increase of malondialdehyde (2.01 +/- 0.03 vs. 1.47 +/- 0.06 micromol/g protein, p<0.05), metallothioneins (1.04 + - 0.22 vs. 0.37 + - 0.06 microg/g, p < 0.05) and 8-oxo-dG concentrations (3.38 + - 0.30 vs.)2.36 +/- 0.28 8-oxo-dG/10(6) bases, p<0.05) in the testis. In the gonad, SMF decreases the CAT (14.33 +/- 1.16 vs. 21.67 +/- 2.05 U/mg protein, p<0.05), GPx (177.40 +/- 5.97 vs. 237.20 +/-15.65 U/mg protein, p<0.05) and mitochondrial Mn-SOD (2.95 +/- 0.10 vs. 3.53 +/- 0.29 U/mg protein, p<0.05) activities. However, cytosolic CuZn-SOD activity is unaffected. CONCLUSIONS: Subchronic exposure to SMF failed to alter spermatogenesis in rat testis. In contrast, the same treatment decreased testosterone levels and induced DNA oxidation.

(E)Aydin M, Cevik A, Kandemir FM, Yuksel M, Apaydin AM. Evaluation of hormonal change, biochemical parameters, and histopathological status of uterus in rats exposed to 50-Hz electromagnetic field. Toxicol Ind Health 25(3):153-158, 2009. (CE, F, OX, VO)

This study investigates the effects of the electromagnetic field (EMF) resulting from the 170 kV high-voltage power lines on hormonal status, on progesterone and 17-beta estradiol levels, and on morphology of the uterus and ovaries associated with biochemical parameters of adult Wistar female rats. The rats were assigned to experimental (21) and control groups (7). The rats in the experimental group were housed in a wooden barn with 7.5 m vertical distance to the power line. Groups 1, 2, and 3 were exposed continuously (24 h) to electric-electromagnetic fields (ELF-EMFs) (48.21 +/- 1.58 mG) for 1, 2, and 3 months, respectively. The rats of group 4 served as the control and were placed in laboratory conditions (The average value of the ELF was 0.75 +/-0.05 V/m. The value of the EMF was calculated to be 0.48 +/- 0.05 mG.). Significant (P < 0.05) decreases were determined among the groups in terms of reproductive organ weights (uterus and ovaries) and progesterone and estrogen levels in relation to the varying periods of the estrous cycle. Although marked reductions (P < 0.05) were observed among the groups in relation to plasma catalase activity, depending on exposure time, no significant differences were found in terms of glutathione and malondialdehyde levels. It is concluded that exposure to the ELF-EMFs for different time periods produced significant decreases in plasma catalase activities in the 3month exposure groups but no effects on progesterone level, on 17-beta estradiol level, or on the morphology and weight of uterus and ovaries.

Bakker JF, Paulides MM, Neufeld E, Christ A, Chen X, Kuster N, Van, Rhoon G. Children and adults exposed to low frequency magnetic fields at the ICNIRP reference levels: Theoretical assessment of the induced electric fields. Phys Med Biol 57:1815-1829, 2012.(Doimetry)

To avoid potentially adverse health effects, the International Commission on Non-Ionizing Radiation Protection (ICNIRP) has defined reference levels for time varying magnetic fields. Restrictions on the electric fields induced in the human body are provided based on biological response data for peripheral nerve stimulation and the induction of phosphenes. Numerical modeling is commonly used to assess the induced electric fields for various exposure configurations. The objective of this study was to assess the variations of the electric fields induced in children and adults and to compare the exposure at reference levels with the basic restrictions as function of anatomy. We used the scalar potential finite element method to calculate the induced electric fields in six children and two adults when exposed to uniform magnetic fields polarized in three orthogonal directions. We found that the induced electric fields are within the ICNIRP basic restrictions in nearly all cases. In PNS tissues, we found electric fields up to 95% (upper uncertainty limit due to discretization errors, k = 2) of the ICNIRP basic restrictions for exposures at the general public reference levels. For occupational reference levels, we found an over-exposure of maximum 79% (k = 2) in PNS tissues. We further found that the ICNIRP recommendations on spatial averaging in $2 \times 2 \times 2$ mm³ contiguous tissue volumes and removal of peak values by the 99th percentile cause the results to depend strongly

on the grid discretization step (i.e. an uncertainty of more than 50% at 2 mm) and the number of distinguished tissues in the anatomical models. The computational results obtained by various research institutes should be robust for different discretization settings and various anatomical models. Therefore, we recommend considering alternative routines for small anatomical structures such as non-contiguous averaging without taking the 99th percentile in future guidelines leading to consistent suppression of peak values amongst different simulation settings and anatomical models. The peak electric fields depend on the local tissue distribution in the various anatomical models, and we could not find a correlation with the size of the anatomy. Therefore, we recommend extending the evaluation using a sufficient set of anatomies including other than standing postures to assess the worst-case exposure setting and correspondence to the basic restrictions.

(E)Bernabò N, Tettamanti E, Pistilli MG, Nardinocchi D, Berardinelli P, Mattioli M, Barboni B. Effects of 50 Hz extremely low frequency magnetic field on the morphology and function of boar spermatozoa capacitated in vitro. Theriogenology. 67(4):801-815, 2007. (AE, FC, I, M, ME, MO)

The aim of this study was to evaluate the effect of an acute exposure to a sinusoidal MF-ELF (50 Hz, 1 mT) on the ability of boar mature spermatozoa to acquire the fertilizing competence in vitro. The spermatozoa exposed during the 4h of incubation to the MF-ELF were evaluated for morphological (surface morphology and acrosome integrity) and functional parameters (cell viability, motility, induction of acrosomal reaction, AR, and the ability to in vitro fertilize oocytes). In parallel, the intracellular Ca(2+) levels as well as the major mechanisms of Ca(2+)clearance were assessed: (45)Ca intakes and intracellular Ca(2+) sequestration by analyzing intracellular Ca(2+) elevation induced by thapsigargin or studying mitochondrial function with Mito-Tracker. The MF-ELF exposure did not affect sperm viability and morphology during the first h of incubation when sperm Ca(2+) homeostasis were already compromised. First of all, MF-ELF treated spermatozoa showed resting intracellular Ca(2+) levels significantly lower than those recorded in controls. This result was dependent on a lower extracellular Ca(2+) intake and from the inhibitory role exerted on both intracellular Ca(2+) storages. As a consequence, after 1h of incubation MF-ELF exposed cells displayed a reduced motility, a modest reactivity when coincubated with solubilized zonae pellucidae and a reduction in oocyte penetrating ability. After 2 or 4h of incubation, in addition, signs of morphological damage appeared on plasma membrane and at acrosomal level. In conclusion, MF-ELF influence negatively spermatozoa first by impairing cell Ca(2+) homeostasis then by dramatically affecting sperm morphology and function.

(E)Bernabò N, Tettamanti E, Russo V, Martelli A, Turriani M, Mattoli M, Barboni B. Extremely low frequency electromagnetic field exposure affects fertilization outcome in swine animal model. Theriogenology. 73(9):1293-1305, 2010. (AE, DE, IV, M, VO)

Modern society continuously exposes the population to electromagnetic radiation, the effects of which on human health, in particular reproduction, are still unknown. The aim of this research was to assess the effect of acute (1h) exposure of boar spermatozoa to a 50 Hz extremely low frequency electromagnetic field (ELF-EMF) on early fertility outcome. The effect of intensities ranging from 0 to 2 mT on morpho-functional integrity of capacitated spermatozoa was examined in vitro. The oviducts containing or without spermatozoa were then exposed to the minimum in vivo, TD(50,) and maximum intensities determined in vitro, 4h before ovulation. The effects of ELF-EMF on spermatozoa in terms of early embryo development were evaluated after 12h and 6 days. It was found that in vitro ELF-EMF > 0.5 mT induced a progressive acrosome damage, thus compromising the ability of spermatozoa to undergo acrosomal reaction after zona pellucida stimulation and reducing the in vitro fertilization outcome. These effects became evident at 0.75 mT and reached the plateau at 1 mT. Under in vivo conditions, the ELF-EMF intensity of 1 mT was able to compromise sperm function, significantly reducing the fertilization rate. In addition, the exposure of oviducts to fields > or = 0.75 mT in the absence of spermatozoa was able to negatively affect early embryo development. In fact, it was found to cause a slowdown in the embryo cleavage. In conclusion, it was demonstrated how and at which intensities ELF-EMF negatively affect early fertility outcome in a highly predictive animal model.

(E)Burcu A, Nevin E, Ilkay A, Amac K, Alper BH, Muge K. The effects of prenatal and postnatal exposure to electromagnetic field on rat ovarian tissue. Toxicol Ind Health 36(12):1010-1018, 2020. (CE, F, IU, MO, OX, PN, VO)

Exposure to an electromagnetic field (EMF) can have adverse effects on many organs and tissues, including the reproductive system. This study aimed to investigate the effects of EMF exposure during prenatal and postnatal periods on ovarian development in rat offspring. In this study, rat pups born from eight pregnant rats were used. EMF exposure was initiated on the first day of pregnancy and continued until the 42nd postnatal day. The blood and ovarian tissue samples of female offspring in sham and EMF groups were collected when they reached the age of 42 days. Follicle-stimulating hormone levels were significantly higher in the EMF group than in the sham group. Estradiol levels were significantly lower in the EMF group than in the sham group. Tissue-inducible nitric oxide synthase (iNOS) levels and expression were significantly greater in the EMF group than in the sham group. In the EMF group, congestion, bleeding areas, and degeneration of follicle structures were observed in ovarian tissue. The findings suggest that exposure to 50-Hz, 3-mT EMF used in this study during prenatal and postnatal periods may lead to impaired ovarian structure and function in female offspring. EMF may affect ovarian physiology by increasing iNOS levels and may lead to fertility disorders.

(E)Cao XW, Zhao TD, Wang CH, Zhou Q, Li LQ, Yao HG, Zhang SQ, Tang JT, Wei W. [Alternating magnetic field damages the reproductive function of murine testes]. Zhonghua Nan Ke Xue. 15(6):530-533, 2009. [Article in Chinese] (AE, M, ME, VO)

OBJECTIVE: To explore the relationship between physical and biological effects of alternating magnetic field and study the influence of the magnetic field on the reproductive function of murine testes. METHODS: Thirty ICR mice were randomized into 5 groups: normal control, X-ray radiation, weak magnetic field (1000 Hz), 1 h strong magnetic field and 2 h strong magnetic field (2000 Hz). The mice were sacrificed at 7 days after the exposure for the analysis of testicular sperm motility, observation of histopathological changes in the testis by HE staining and evaluation of the changes by modified Johnsen grade criteria. RESULTS: The rates of sperm motility were (42.37 +/-10.24)% in the normal control group, (39.00 +/-12.35)% in the X-ray radiation group, (36.00 +/-17.28)% in the weak magnetic field group, (10.72 +/-5.67)% in the 1 h strong magnetic field group and (4.44 +/-2.87)% in the 2 h strong magnetic field group, respectively. Johnsen's scores decreased and the testis damage increased in a dose- and time-dependent manner. CONCLUSION: Magnetic field, either strong or weak, may damage the testis function by inducing injury to seminiferous tubules and Leydig cells, thickening of the basal membrane, derangement, exfoliation, massive apoptosis and necrosis of sperm.

(E)Cecconi S, Gualtieri G, Di Bartolomeo A, Troiani G, Cifone MG, Canipari R. Evaluation of the effects of extremely low frequency electromagnetic fields on mammalian follicle development. Hum Reprod 15(11):2319-2325, 2000. (CE, F, ME, IV)

The aim of this study was to evaluate the effects of pulsed, extremely low-frequency electromagnetic fields (ELF-EMF) on in-vitro mouse pre-antral follicle development. Pre-antral follicles were cultured for 5 days and exposed to ELF-EMF at the frequencies of 33 or 50 Hz. ELF-EMF application did not affect follicular growth over a 3 day culture period, but on day 5 the growth of 33 Hz-exposed follicles was significantly reduced when compared with controls, while the 50 Hz-exposed follicles were not significantly affected. However, ELF-EMF severely impaired antrum formation at both frequencies, as 79 +/- 3% of control follicles respectively. The follicles with failed antrum formation showed lower oestradiol release and granulosa cell DNA synthesis, but these effects were not related to granulosa cell apoptosis. Furthermore, a high percentage of the in-vitro grown oocytes obtained from exposed follicles had a reduced ability to resume meiotic maturation when compared with controls. These results suggest that ELF-EMF exposure might impair mammalian female reproductive potentiality by reducing the capacity of the follicles to reach a developmental stage that is an essential pre-requisite for reproductive success.

Cech R, Leitgeb N, Pediaditis M. Fetal exposure to low frequency electric and magnetic fields. Phys Med Biol 52:879-888, 2007. (Dosimetry)

To investigate the interaction of low frequency electric and magnetic fields with pregnant women and in particular with the fetus, an anatomical voxel model of an 89 kg woman at week 30 of pregnancy was developed. Intracorporal electric current density distributions due to exposure to homogeneous 50 Hz electric and magnetic fields were calculated and results were compared with basic restrictions recommended by ICNIRP guidelines. It could be shown that the basic restriction is met within the central nervous system (CNS) of the mother at exposure to reference level of either electric or magnetic fields. However, within the fetus the basic restriction is considerably exceeded. Revision of reference levels might be necessary.

Cech R, Leitgeb N, Pediaditis M. Current densities in a pregnant woman model induced by simultaneous ELF electric and magnetic field exposure. Phys Med Biol 53(1):177-186, 2008. (Dosimetry)

The pregnant woman model SILVY was studied to ascertain to what extent the electric current densities induced by 50 Hz homogeneous electric and magnetic fields increase in the case of simultaneous exposure. By vectorial addition of the electric current densities, it could be shown that under worst case conditions the basic restrictions recommended by ICNIRP (International Commission on Non-Ionizing Radiation Protection) guidelines are exceeded within the central nervous system (CNS) of the mother, whereas in sole field exposure they are not. However, within the foetus the induced current densities do not comply with basic restrictions, either from single reference-level electric fields or from simultaneous exposure to electric and magnetic fields. Basic limits were considerably exceeded.

(NE)Chung MK, Lee SJ, Kim YB, Park SC, Shin DH, Kim SH, Kim JC. Evaluation of spermatogenesis and fertility in F1 male rats after in utero and neonatal exposure to extremely low frequency electromagnetic fields. Asian J Androl. 7(2):189-194, 2005.(CE, DE, IU, M, PN, VO)

AIM: To determine whether in utero and neonatal exposure to a 60 Hz extremely low frequency electromagnetic field (EMF) results in spermatotoxicity and reproductive dysfunction in the F1 offspring of rats. METHODS: Age-matched, pregnant Sprague-Dawley rats were exposed continuously (21 h/day) to a 60 Hz EMF at field strengths of 0 (sham control), 5, 83.3 or 500 microT from day 6 of gestation through to day 21 of lactation. The experimentally generated magnetic field was monitored continuously (uninterrupted monitoring over the period of the study) throughout the study. RESULTS: No exposure-related changes were found in exposed or sham-exposed animals with respect to the anogenital distance, preputial separation, testis weight, testicular histology, sperm count, daily sperm production, sperm motility, sperm morphology and reproductive capacity of F1 offspring. CONCLUSION: Exposure of Sprague-Dawley rats to a 60 Hz EMF at field strengths of up to 500 microT from day 6 of gestation to day 21 of lactation did not produce any detectable alterations in offspring spermatogenesis and fertility.

(E)De Vita R, Cavallo D, Raganella L, Eleuteri P, Grollino MG, Calugi A. Effects of 50 Hz magnetic fields on mouse spermatogenesis monitored by flow cytometric analysis. Bioelectromagnetics. 16(5):330-334, 1995. (AE, M, ME, VO)

Flow cytometry (FCM) was performed to monitor the cellular effects of extremely-lowfrequency magnetic field on mouse spermatogenesis. Groups of five male hybrid F1 mice aged 8-10 weeks were exposed to 50 Hz magnetic field. The strength of the magnetic field was 1.7 mT. Exposure times of 2 and 4 h were chosen. FCM measurements were performed 7, 14, 21, 28, 35, and 42 days after treatment. For each experimental point, a sham-treated group was used as a control. The possible effects were studied by analyzing the DNA content distribution of the different cell types involved in spermatogenesis and using the elongated spermatids as the reference population. The relative frequencies of the various testicular cell types were calculated using specific software. In groups exposed for 2 h, no effects were observed. In groups exposed for 4 h, a statistically significant (P < 0.001) decrease in elongated spermatids was observed at 28 days after treatment. This change suggests a possible cytotoxic and/or cytostatic effect on differentiating spermatogonia. However, further studies are being carried out to investigate the effects of longer exposure times.

(E)de Vocht F, Hannam K, Baker P, Agius R. Maternal residential proximity to sources of extremely low frequency electromagnetic fields and adverse birth outcomes in a UK cohort. Bioelectromagnetics 35(3):201-209, 2014. (CE, DE, HU, IU)

Studies have suggested that exposure to extremely low frequency electromagnetic fields (ELF-EMF) may be associated with increased risk of adverse birth outcomes. This study tested the hypothesis that close proximity to residential ELF-EMF sources is associated with a reduction in birth weight and increased the risk of low birthweight (LBW), small for gestational age (SGA) and spontaneous preterm birth (SPTB). Closest residential proximity to high voltage cables, overhead power lines, substations or towers during pregnancy was calculated for 140356 singleton live births between 2004 and 2008 in Northwest England. Associations between proximity and risk for LBW, SGA and SPTB were calculated, as well as associations with birth weight directly. Associations were adjusted for maternal age, ethnicity, parity and for part of the population additionally for maternal smoking during pregnancy. Reduced average birth weight of 212 g (95% confidence interval (CI): -395 to -29 g) was found for close proximity to a source, and was largest for female births (-251 g (95% CI: -487 to -15 g)). No statistically significant increased risks for any clinical birth outcomes with residential proximity of 50 m or less were observed. Living close (50 m or less) to a residential ELF-EMF source during pregnancy is associated with suboptimal growth in utero, with stronger effects in female than in males. However, only a few pregnant women live this close to high voltage cables, overhead power lines, substations or towers, likely limiting its public health impact.

(E)de Vocht F, Lee B. Residential proximity to electromagnetic field sources and birth weight: Minimizing residual confounding using multiple imputation and propensity score matching. Environ Int 69:51-57, 2014. (CE, DE, HU, IU)

Studies have suggested that residential exposure to extremely low frequency (50 Hz) electromagnetic fields (ELF-EMF) from high voltage cables, overhead power lines, electricity substations or towers are associated with reduced birth weight and may be associated with adverse birth outcomes or even miscarriages. We previously conducted a study of 140,356 singleton live births between 2004 and 2008 in Northwest England, which suggested that close residential proximity (\leq 50 m) to ELF-EMF sources was associated with reduced average birth weight of 212 g (95%CI: -395 to -29 g) but not with statistically significant increased risks for other adverse perinatal outcomes. However, the cohort was limited by missing data for most

potentially confounding variables including maternal smoking during pregnancy, which was only available for a small subgroup, while also residual confounding could not be excluded. This study, using the same cohort, was conducted to minimize the effects of these problems using multiple imputation to address missing data and propensity score matching to minimize residual confounding. Missing data were imputed using multiple imputation using chained equations to generate five datasets. For each dataset 115 exposed women (residing \leq 50 m from a residential ELF-EMF source) were propensity score matched to 1150 unexposed women. After doubly robust confounder adjustment, close proximity to a residential ELF-EMF source remained associated with a reduction in birth weight of -116 g (95% confidence interval: -224:-7 g). No effect was found for proximity \leq 100 m compared to women living further away. These results indicate that although the effect size was about half of the effect previously reported, close maternal residential proximity to sources of ELF-EMF remained associated with suboptimal fetal growth.

(NE)Diebolt JR. The influence of electrostatic and magnetic fields on mutation in Drosophila melanogaster spermatozoa. Mutat Res. 57(2):169-174, 1978. (AE, GE, M, VO)

Canton-S Drosophila melanogaster males were exposed to electrostatic and magnetic fields for 24 h to determine the influence of low energy fields on the production of sex-linked recessive lethal mutations in the mature, motile sperm. To detect sex-linked recessive lethal production in mature sperm the standard Muller-5 test was done. Exposure of the males to the magnetic field or the electrostatic field did not significantly affect the mutation frequency in mature sperm.

(E)Drozdov KA, Khlistun OA, Drozdov AL. [The influence of ultrasound and constant magnetic field on gametes, zygotes, and embryos of the sea urchin]. Biofizika. 53(3):513-518, 2008. [Article in Russian] (AE, F, M, ME, VO)

The influence of constant magnetic field, power 7 T, and ultrasound, frequency 2, 4 and 8 MHz, on gametes, fertization, embryos and larvae of the sea urchin was studied. It was shown that magnetic field breaks the process of the gamete fusion but does not influence gametes, embryos, and larvae. Ultrasound impairs the motility of spermatozoa and larvae, prevents the fertilization, and breaks the embryonic development. It is assumed that the effect of the magnetic field is connected with the response of the cortical cytoskeleton, which consists of bundles of actin microfilaments. The rearrangement of the cortical cytoskeleton occurs during the first 20 minutes after the contact of sperm with the egg. Also there is effect of magnetic fields on calcium ions, which are liberated during the first seconds after gamete contact. The effect of the ultrasound is explained by a small increase in water temperature and cavitation process, which break cellular structures.

(E)Drzewiecka EM, Kozlowska W, Paukszto L, Zmijewska A, Wydorski PJ, JP, Franczak A. Effect of the Electromagnetic Field (EMF) Radiation on Transcriptomic Profile of Pig Myometrium during the Peri-Implantation Period-An In Vitro Study. Int J Mol Sci 22(14):7322, 2021. (AE, F, GE, IV)

The electromagnetic field (EMF) affects the physiological processes in mammals, but the molecular background of the observed alterations remains not well established. In this study was tested the effect of short duration (2 h) of the EMF treatment (50 Hz, 8 mT) on global transcriptomic alterations in the myometrium of pigs during the peri-implantation period using next-generation sequencing. As a result, the EMF treatment affected the expression of 215 transcript active regions (TARs), and among them, the assigned gene protein-coding biotype possessed 90 ones (differentially expressed genes, DEGs), categorized mostly to gene ontology terms connected with defense and immune responses, and secretion and export. Evaluated DEGs enrich the KEGG *TNF signaling pathway*, and *regulation of IFNA signaling* and *interferon-alpha/beta signaling* REACTOME pathways. There were evaluated 12 differentially expressed long non-coding RNAs (DE-Inc-RNAs) and 182 predicted single nucleotide variants (SNVs) substitutions within RNA editing sites. In conclusion, the <u>EMF treatment in the myometrium</u> collected during the peri-implantation period affects the expression of genes involved in defense and immune responses. The study also gives new insight into the mechanisms of the EMF action in the regulation of the transcriptomic profile through lnc-RNAs and SNVs.

(E)Duan W, Liu C, Zhang L, He M, Xu S, Chen C, Pi H, Gao P, Zhang Y, Zhong M, Yu Z, Zhou Z. Comparison of the genotoxic effects induced by 50 Hz extremely low-frequency electromagnetic fields and 1800 MHz radiofrequency electromagnetic fields in GC-2 cells. Radiat Res 183(3):305-314, 2015. (AE, GE, IV, M)

Extremely low-frequency electromagnetic fields (ELF-EMF) and radiofrequency electromagnetic fields (RF-EMF) have been considered to be possibly carcinogenic to humans. However, their genotoxic effects remain controversial. To make experiments controllable and results comparable, we standardized exposure conditions and explored the potential genotoxicity of 50 Hz ELF-EMF and 1800 MHz RF-EMF. A mouse spermatocyte-derived GC-2 cell line was intermittently (5 min on and 10 min off) exposed to 50 Hz ELF-EMF at an intensity of 1, 2 or 3 mT or to RF-EMF in GSM-Talk mode at the specific absorption rates (SAR) of 1, 2 or 4 W/kg. After exposure for 24 h, we found that neither ELF-EMF nor RF-EMF affected cell viability using Cell Counting Kit-8. Through the use of an alkaline comet assay and immunofluorescence against γ -H2AX foci, we found that ELF-EMF exposure resulted in a significant increase of DNA strand breaks at 3 mT, whereas RF-EMF exposure had insufficient energy to induce such effects. Using a formamidopyrimidine DNA glycosylase (FPG)-modified alkaline comet assay, we observed that RF-EMF exposure significantly induced oxidative DNA base damage at a SAR value of 4 W/kg, whereas ELF-EMF exposure did not. Our results suggest that both ELF-EMF and RF-EMF under the same experimental conditions may produce genotoxicity at relative high intensities, but they create different patterns of DNA damage. Therefore, the potential mechanisms underlying the genotoxicity of different frequency electromagnetic fields may be different.

(E)Dundar B, Cesur G, Comlekci S, Songur A, Gokcimen A, Sahin O, Ulukut O, Ramazan Yilmaz H, Sutcu R, Caliskan S. The effect of the prenatal and post-natal long-term exposure to 50 Hz electric field on growth, pubertal development and IGF-1 levels in female Wistar rats. Toxicol Ind Health 25(7):479-487, 2009. (CE, DE, F, IU, ME, PN, VO) electric field

To investigate prenatal and post-natal effects of extremely low frequency (ELF) electric field (EF) on growth and pubertal development, pregnant Wistar rats were randomly distributed among three groups. The pregnant rats of the prenatal group were exposed to 24-hour EF at 50 Hz EF 10 kV/min during pregnancy and their subsequent randomly selected female pups continued to be exposed until puberty. The post-natal group was unexposed to EF during pregnancy, but randomly selected female pups from this group were exposed to EF between delivery and puberty at the same doses and duration as the prenatal group. The third group was a sham-exposed group. The mean birth weight and weight gain of the pups during study period were found significantly reduced in prenatal group than post-natal and sham-exposed groups (p < p0.001). No difference could be found among the three groups for body weight at puberty (p > 0.05). The mean age at vaginal opening and estrous were significantly higher at prenatal group than post-natal and sham-exposed groups (p < 0.001). Serum insulin-like growth hormone-1 (IGF-1) levels were found significantly reduced in prenatal exposure group compared with the other two groups (p < 0.001). There was no difference for birth weight, weight gain, the mean age at vaginal opening and estrous and IGF-1 levels between post-natal and sham-exposed groups (p > 0.05). There was also no difference for FSH, LH and E2 levels at puberty among the three groups (p > 0.05). Histological examination revealed that both the prenatal and post-natal groups had the evidence of tissue damage on hypothalamus, pituitary gland and ovaries. In conclusion, early beginning of prenatal exposure of rats to 24 hours 50 Hz EF at 10 kV/m until puberty without magnetic field (MF) resulted in growth restriction, delayed puberty and reduced IGF-1 levels in female Wistar rats. These effects probably associated with direct toxic effects of EF on target organs. Post-natal exposure to EF at similar doses and duration seems to be less harmful on target organs. Post-natal exposure to EF at similar doses and duration seems to be less harmful.

(E)Emura R, Ashida N, Higashi T, Takeuchi T. Orientation of bull sperms in static magnetic fields. Bioelectromagnetics. 22(1):60-65, 2001. (M, sperm orientation in magnetic field)

The orientation of bull sperm cells in static magnetic fields was investigated by microscopic observation. The bull sperm, which has a very flat head, was fixed and its motion was stopped by glutaraldehyde. It was oriented with the whole body and the flat head perpendicular to the direction of the magnetic field. The diamagnetic cell components, such as the cell membrane, the DNA in the head, and the microtubule in the tail, were thought to contribute to this orientation, because bull sperm does not have paramagnetic components. For quantitative measurement of the orientation, the intensity of transmitted light through glutaraldehyde-fixed bull sperm suspension in a photometric cell was determined. The intensity changed slightly in proportion to the mean degree of orientation of the sperms. It increased sigmoidally depending on the intensity of the magnetic field and reached 100% at just below 1 T. The magnetic orientation is very strong in comparison to that of erythrocytes or platelets. By studying the response of the bull sperm to the magnetic field, it will be possible to understand its microstructure in more detail.

(E)Ersoy N, Acikgoz B, Aksu I, Kiray A, Bagriyanik HA, Kiray M. The Effects of Prenatal and Postnatal Exposure to 50-Hz and 3 mT Electromagnetic Field on Rat Testicular Development. Medicina (Kaunas) 59(1):71, 2022.(CE, IU, M, ME, MO, OX, PN, VO)

Background and objectives: It has been shown that electromagnetic fields (EMFs) have negative effects on the reproductive system. The biological effects of EMF on the male reproductive system are controversial and vary depending on the frequency and exposure time. Although a limited number of studies have focused on the structural and functional effects of EMF, the effects of prenatal and postnatal EMF exposure on testes are not clear. We aimed to investigate the effects of 50-Hz, 3-mT EMF exposure (5 days/wk, 4 h/day) during pre- and postnatal periods on testis development. *Materials and Methods:* Pups from three groups of Sprague-Dawley pregnant rats were used: Sham, EMF-28 (EMF-exposure applied during pregnancy and until postnatal day 28), EMF-42 (EMF-exposure applied during pregnancy and until postnatal day 42). The testis tissues and blood samples of male offspring were collected on the postnatal day 42. Results: Morphometric analyses showed a decrease in seminiferous tubule diameter as a result of testicular degeneration in the EMF-42 group. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were decreased in the EMF-42 group. Lipid peroxidation levels were increased in both EMF groups, while antioxidant levels were decreased only in the EMF-28 group. We found decreased levels of vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF1) in the EMF-42 group, and decreased levels of the SRC homology 3 (SH3) and multiple ankyrin repeat domain (SHANK3) in the EMF-28 group in the testis tissue. Conclusions: EMF exposure during pre- and postnatal periods may cause deterioration in the structure and function of testis and decrease in growing factors that would affect testicular functions in male rat pups. In addition to the oxidative stress observed in testis, decreased SHANK3, VEGF, and IGF1 protein levels suggests that these proteins may be mediators in testis affected by EMF exposure. This study shows that EMF exposure during embryonic development and adolescence can cause apoptosis and structural changes in the testis.

(NE)

Eskelinen T, Roivainen P, Mäkelä P, Keinänen J, Kauhanen O, Saarikoski S, Juutilainen J. Maternal exposure to extremely low frequency magnetic fields: Association with time to pregnancy and foetal growth. Environ Int 94:620-625, 2016.(CE, DE, HU, IU, ME)

Background: Data on reproductive and developmental effects of extremely low frequency magnetic fields (ELF MFs) are inconclusive. This study tested the hypothesis that maternal exposure to ELF MFs is associated with increased time to pregnancy (TTP), reduced birthweight or small for gestational age (SGA). **Methods:** The study cohort consisted of 373 mothers who gave birth between 1990 and 1994 in Kuopio University Hospital, Finland. To increase prevalence of high ELF MF exposure, women living in buildings near known ELF MF sources were included. Maternal exposure to ELF MF before and during pregnancy was assessed with short term measurements in residences and questionnaires. Associations between ELF MF exposure and TTP, low birth weight and SGA were analysed by logistic regression (or linear regression for continuous variables), adjusting for factors known to be associated with the selected pregnancy outcomes, such as maternal smoking, alcohol consumption and socioeconomic status. **Results:** The MF exposure of the mothers was slightly higher than in Finnish residences in general, but very high exposures (>0.4 µT) were rare. No consistent association of ELF MF with TTP, birth weight or SGA was found. **Conclusions:** ELF MF

exposure is not likely to be associated with TTP or prenatal growth at residential exposure levels that were observable in this study.

(E) Esmailzadeh S, Delavar MA, Aleyassin A, Gholamian SA, Ahmadi A. Exposure to Electromagnetic Fields of High Voltage Overhead Power Lines and Female Infertility. Int J Occup Environ Med 10(1):11-16, 2019. (CE, F, FC, HU)

Background: Living in the vicinity of high voltage power lines has brought about a range of health woes, but the effect of residential exposure to electromagnetic fields from the power lines on female fertility has not been explored yet. Objective: To test the hypothesis if residential proximity to high voltage power lines could be associated with the increased risk of female infertility. Methods: In a case-control study, 462 women with confirmed diagnosis of unexplained infertility or behavioral and environmental factors were assessed between February 2014 and December 2016. Control group comprised of 471 persons with no history of infertility selected using randomized-digit dialing from the numbers registered in a birth registry between 2014 and 2016. The nearest linear distance from high voltage power lines to the participants' residence of cases and controls was measured using a Geographical Information System (GIS) and Google Earth aerial evaluation for high voltage power lines (240-400 kV). Results: 112 (14.1%) houses were within 500 meters from a high voltage power line. Women living within 500 meters of the lines (OR 4.14, 95% CI 2.61 to 6.57) and 500-1000 meters of the line (OR 1.61, 95% CI 1.05 to 2.47) carried a significantly higher risk of infertility than those women living more than 1000 meters away from the power lines. After adjusting for confounding factors, women living within 500 meters of the lines carried a higher risk (aOR 4.44, 95% CI 2.77 to 7.11) of infertility compared with women living more than 1000 meters of the lines. Conclusion: The current safety guidelines for electromagnetic fields exposure seems to be not adequate for protecting people from the hazardous effects of the field.

Fiocchi S, Chiaramello E, Parazzini M, Ravazzani P. Influence of tissue conductivity on foetal exposure to extremely low frequency magnetic fields at 50 Hz using stochastic dosimetry. PLoS One 13(2):e0192131, 2018. (Dosimetry)

Human exposure to extremely low frequency magnetic fields (ELF-MF) at 50 Hz is still a topic of great interest due to the possible correlation with childhood leukaemia. The estimation of induced electric fields in human tissues exposed to electromagnetic fields (EMFs) strictly depends on several variables which include the dielectric properties of the tissues. In this paper, the influence of the conductivity assignment to foetal tissues at different gestational ages on the estimation of the induced electric field due to ELF-MF exposure at 50 Hz has been quantified by means of a stochastic approach using polynomial chaos theory. The range of variation in conductivity values for each foetal tissue at each stage of pregnancy have been defined through three empirical approaches and the induced electric field in each tissue has been modelled through stochastic dosimetry. The main results suggest that both the peak and median induced electric field induced in foetal brain does not seem to be significantly affected by conductivity data changes. The maximum exposure levels, in terms of the induced electric field found in each

specific tissue, were found to be significantly below the basic restrictions indicated in the ICNIRP Guidelines, 2010.

(E) Franczak A, Waszkiewicz EM, Kozlowska W, Zmijewska A, Koziorowska A. Consequences of electromagnetic field (EMF) radiation during early pregnancy - androgen synthesis and release from the myometrium of pigs in vitro. Anim Reprod Sci 218:106465, 2020. (AE, GE, F, IV)

An electromagnetic field (EMF) has been found to affect reproductive processes in females. The aim of this study was to determine the effect of low, non-ionizing EMF radiation on the steroidogenic activity of myometrium collected from pigs during the fetal peri-implantation period. Myometrial slices were treated with an EMF (50 and 120 Hz, 2 and 4 h of incubation) and examined for the aromatase cytochrome P450 17a-hydroxylase/C17-20lyase (CYP17A1) and 3 β -hydroxysteroid dehydrogenase/ Δ 5- Δ 4 isomerase (HSD3B1) mRNA transcript abundance, cytochrome P450c17 and 3BHSD protein abundance and the secretion of androstenedione (A4) and testosterone (T). To determine whether progesterone (P4) functions as a protectant from EMF radiation, the selected slices were treated with P4. In slices incubated without P4, EMF at 50 Hz altered cytochrome P450c17 protein abundance (4 h), HSD3B1 mRNA transcript abundance (4 h) and A4 release (2 h) as well as T release (2 h) in P4-treated slices. The EMF at 120 Hz in non P4-treated slices altered A4 release (2 and 4 h) whereas in P4treated slices altered CYP17A1 mRNA transcript abundance (4 h), 3BHSD protein abundance (4 h), A4 (4 h) and T release (2 h). In conclusion, EMF radiation in the myometrium collected during the peri-implantation period alters the CYP17A1 and HSD3B1 mRNA transcript and encoded protein abundance, and androgen release due to the time of treatment and P4 presence or absence. The P4 did not function directly as an obvious protector against EMF radiation in the myometrium of pigs during the fetal peri-implantation period.

(E)Furuya H, Aikawa H, Hagino T, Yoshida T, Sakabe K. [Flow cytometric analysis of the effects of 50 Hz magnetic fields on mouse spermatogenesis]. Nihon Eiseigaku Zasshi. 53(2):420-425, 1998. [Article in Japanese] (CE, M, ME, MO, VO)

The cellular effects of an extremely-low-frequency (ELF) magnetic field on mouse spermatogenesis were assessed by DNA flow cytometry and serum testosterone. Seven week old male ICR mice were exposed to a 50 Hz magnetic field the strength of which was 1.0 m Tesla. Seven mice per treatment group were exposed for 13, 26, 39 or 52 days. For each experimental point, an equal number of mice per sham-treated group were used as a control and were exposed only to the background field below 1 mu Tesla in the same room as the treatment group. In the control mice, the testis cellular DNA content distribution by flow cytometory was characterized by four quantifiable populations; round spermatids (1C), spermatogonia and other diploid cells (2C), spermatogonial cells synthesizing DNA (S-phase) and primary spermatocytes (4C). In animals exposed for 26 days the number of cells in the 4C and the 4C:2C ratio was significantly lower, and the 1C:4C ratio (meiotic transformation) was significantly higher than the corresponding control groups. In animals exposed for 52 days the cell population in 1C and the 1C:2C ratio (total germ-cell transformation) was significantly higher, and the cell population in 2C was significantly lower than the corresponding control groups. The concentration of serum testosterone in animals exposed for 13 days was significantly higher than in the corresponding control group. <u>These changes suggest that long-term exposure to an ELF magnetic field had a</u> possible effect on the proliferation and differentiation of spermatogonia.

(E) Gholami D, Riazi G, Fathi R, Sharafi M, Shahverdi A. Comparison of polymerization and structural behavior of microtubules in rat brain and sperm affected by the extremely low-frequency electromagnetic field. BMC Mol Cell Biol 20(1):41, 2019. (CE, FC, M, MO, VO)

Background: Microtubule proteins are able to produce electromagnetic fields and have an important role in memory formation, and learning. Therefore, microtubules have the potential to be affected by exogenous electromagnetic fields. This study aimed to examine the comparison of microtubule polymerization and its structural behavior in brain and sperm affected by 50 Hz extremely low-frequency electromagnetic field (ELEF). Results: Twenties adult male rats were randomly and equally divided into control and experimental groups, to evaluate the effect of 50 Hz ELEF on the sperm and brain functions. Plus-maze, serum testosterone and corticosterone, and sperm evaluation were performed. Next, the semen and brain samples were obtained, and they were divided into four experimental groups for investigation of microtubule polymerization. There was no significant difference in testosterone and, corticosterone levels, anxiety behaviors, and sperm morphology between control and ELEF-exposure groups. The sperm viability, total and progressive motility were significantly higher in the ELEF-exposed group than that of the control group. The microtubule polymerization in sperm ELEF was significantly higher than in other groups. The secondary and tertiary structures of tubulins were significantly affected in the brain, and sperm ELEF groups. Conclusion: It seems that the polymerization of microtubules and conformational changes of tubulin dimers are improved by ELEF application.

(E)Górski R, Kotwicka M, Skibińska I, Jendraszak M, Wosiński S. Effect of lowfrequency electric field screening on motility of human sperm. Ann Agric Environ Med 27(3):427-434, 2020. (AE, FC, M, IV)

Introduction: The human body is constantly exposed to an extremely low electromagnetic field (ELF-EMF), in particular at 50 Hz, emitted by power lines, domestic distribution lines, electrical appliances, etc. It is assumed that the increase in electromagnetic exposure may cause adverse effects upon human health, as well as raising concerns regarding the impact on human fertility. **Objective:** The aim of this in vitro study was to investigate the influence of ELF-EMF with a frequency of 50 Hz on the motility of human sperm. At the same time, the effectiveness of the dielectric screen constructed by ADR Technology ® in absorbing the emitted radiation was examined. Material and methods: Semen samples of 20 patients were exposed to the influence of an extremely low electromagnetic field. After 5, 15 and 30 min., spermatozoa motility was analysed using a computer-assisted spermatozoa motility analysis system. The following sperm motility parameters were examined: 1) velocity straight linear motility; 2) cross-beat frequency; 3) lateral head displacement; 4) homogeneity of progressive motility velocity. Results: It was found that the ELF-EMF presented a negative effect on the motility of human spermatozoa. A significant decrease in spermatozoa motility speed and a significant increase in lateral head deviation values were observed under the influence of the electromagnetic field. ELF-EMF did not show an effect on either lateral head displacement or homogeneity of progressive motility

velocity. **Conclusions:** A positive effect of the dielectric screen ADR Technology® was found. This effect compensated spermatozoa motility changes induced with ELF-EMF.

(E)Guo Y, Fu Y, Sun W. 50 Hz Magnetic Field Exposure Inhibited Spontaneous Movement of Zebrafish Larvae through ROS-Mediated syn2a Expression. Int J Mol Sci 24(8):7576, 2023. (CE, GE, FC, IU, ME, MO, OX)

Extremely low frequency electromagnetic field (ELF-EMF) exists widely in public and occupational environments. However, its potential adverse effects and the underlying mechanism on nervous system, especially behavior are still poorly understood. In this study, zebrafish embryos (including a transfected synapsin IIa (syn2a) overexpression plasmid) at 3 h postfertilization (hpf) were exposed to a 50-Hz magnetic field (MF) with a series of intensities (100, 200, 400 and 800 µT, respectively) for 1 h or 24 h every day for 5 days. Results showed that, although MF exposure did not affect the basic development parameters including hatching rate, mortality and malformation rate, yet MF at 200 µT could significantly induce spontaneous movement (SM) hypoactivity in zebrafish larvae. Histological examination presented morphological abnormalities of the brain such as condensed cell nucleus and cytoplasm, increased intercellular space. Moreover, exposure to MF at 200 µT inhibited syn2a transcription and expression, and increased reactive oxygen species (ROS) level as well. Overexpression of syn2a could effectively rescue MF-induced SM hypoactivity in zebrafish. Pretreatment with Nacetyl-L-cysteine (NAC) could not only recover syn2a protein expression which was weakened by MF exposure, but also abolish MF-induced SM hypoactivity. However, syn2a overexpression did not affect MF-increased ROS. Taken together, the findings suggested that exposure to a 50-Hz MF inhibited spontaneous movement of zebrafish larvae via ROS-mediated syn2a expression in a nonlinear manner.

Habash M, Gogna P, Krewski D, Habash RWY. Scoping Review of the Potential Health Effects of Exposure to Extremely Low-Frequency Electric and Magnetic Fields. Crit Rev Biomed Eng 47(4):323-347, 2019. (Review)

Previous studies suggest that extremely low-frequency (ELF) electric and magnetic fields (EMFs) may impact human health. However, epidemiologic studies have provided inconsistent results on the association between exposure to ELF EMFs and various health outcomes. This scoping review reports on primary investigations that were published during the ten-year period of 2007-2017 on the association between ELF EMFs and cancer, cardiovascular disease (CVD), reproductive health effects, and neurodegenerative diseases. We identified a total of 361 articles from two bibliographic databases (PubMed and EMBASE). Of these, 39 articles (19 cancer studies, two CVD studies, nine reproductive health studies, and ten neurodegenerative disease studies [with one repeated for two outcomes]) met inclusion criteria. Articles identified in this study focus on three different types of exposure: occupational (22 studies), residential (15 studies), and electric blanket (two studies). This review suggests that ELF EMFs may be associated with neurodegenerative diseases, specifically Alzheimer's disease; however, limited evidence was found to suggest that ELF EMFs are associated with several types of cancer, CVD, and reproductive outcomes. Additional epidemiological studies in large study populations with improved exposure assessments are needed to clarify current inconclusive relationships.

(NE)Heredia-Rojas JA, Caballero-Hernandez DE, Rodriguez-de la Fuente AO, Ramos-Alfano G, Rodriguez-Flores LE. Lack of alterations on meiotic chromosomes and morphological characteristics of male germ cells in mice exposed to a 60 Hz and 2.0 mT magnetic field. Bioelectromagnetics. 25(1):63-68, 2004. (CE, GE, M, ME, VO)

The effect of in vivo exposure of mice to a 60 Hz sinusoidal magnetic field (MF) at 2.0 mT on male germ cells was studied. The cytological endpoints measured included meiotic chromosome aberrations in spermatocytes and sperm morphology. Three independent experiments were carried out: (a) animals exposed for 72 h, (b) 10 days/8 h daily, and (c) 72 h exposure to MF plus 5 mg/kg of Mitomycin-C. No statistically significant differences indicative of MF effects were observed between MF exposed and control animals. In addition, an opposite effect between MF exposure and Mitomycin-C treatment in terms of chromosomal aberrations and sperm morphology was observed.

(E)Hong R, Liu Y, Yu YM, Hu K, Weng EQ. [Effects of extremely low frequency electromagnetic fields on male reproduction in mice]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 21(5):342-345, 2003. [Article in Chinese] (CE, DE, FC, M, ME, VO)

OBJECTIVE: To investigate the effects of extremely low frequency electromagnetic fields (ELF EMFs) on male reproduction in mice. METHODS: 94 adult male mice were exposed to 50 Hz sinusoidal electromagnetic fields of 0.2, 3.2 or 6.4 mT for 2 weeks or 4 weeks. Testicular histology and weight, sperm amount, sperm motility and morphology were measured. The percentages of different ploidy cells and cell phases, and DNA content of testis cells were estimated by flow cytometry. The micronucleus rate of bone-marrow cell was also observed. RESULTS: The testicular weight of the mice exposed to 6.4 mT for 4 weeks [(76.06 +/- 32.25) mg] was significantly lower than that of the control [(111.44 +/- 19.99) mg, P < 0.05]; no significant histopathological changes were observed on the testis in EMFs exposed mice; the sperm amount was decreased after EMFs exposure for 4 weeks, and those of the mice exposed to 0.2 mT and 6.4 mT for 4 weeks $[(4.87 + -0.94) \times 10(6)/m]$ and $(4.30 + -1.89) \times 10(6)/m]$ respectively] were significantly lower than that of the control [(6.67 ± 0.70) x 10(6)/ml, P < 0.05]; the rates of sperm motility also showed a decline. After 0.2, 3.2 or 6.4 mT EMFs exposure for 2 weeks, the deformity rates of sperm [(7.416 +/- 3.352)%, (6.862 +/- 2.947)% and (8.112 +/-4.615)% respectively] were significantly higher than that of the control [(4.098 +/- 2.028)%, P < 0.01]. Similarly, those of the mice exposed for 4 weeks [(10.267 + 3.836)), (11.027 + - (8.814 ± 3.678) % respectively] were higher than that of the control $((3.714 \pm 7.059))$ % 1.830)%]. After 6.4 mT exposure for 2 weeks, the percentages of 1C testis cells [(69.56 +/-(4.07) was significantly lower than that of the control [(73.45 + 3.10)%, P < 0.05]. There were not any remarkable changes in those of 2C, 4C cells. DNA content in different ploidy cells of the mice exposed to 6.4 mT was decreased. Moreover, the cell percentage in S phase was increased significantly (P < 0.01). CONCLUSION: ELF EMFs exposure may have some adverse effects on reproduction in mice.

(E)Hong R, Zhang Y, Liu Y, Weng EQ. [Effects of extremely low frequency electromagnetic fields on DNA of testicular cells and sperm chromatin structure in mice]. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 23(6):414-417, 2005. [Article in Chinese] (CE, GE, M, VO)

OBJECTIVE: To study the effects of 50 Hz electromagnetic fields (EMFs) on DNA of testicular cells and sperm chromatin structure in mice. METHODS: Mice were exposed to 50 Hz, 0.2 mT or 6.4 mT electromagnetic fields for 4 weeks. DNA strand breakage in testicular cells was detected by single-cell gel electrophoresis assay. Sperm chromatin structure was analyzed by sperm chromatin structure assay with flow cytometry. RESULTS: After 50 Hz, 0.2 mT or 6.4 mT EMFs exposure, the percentage of cells with DNA migration in total testicular cells increased from the control level of 25.64% to 37.83% and 39.38% respectively. The relative length of comet tail and the percentage of DNA in comet tail respectively increased from the control levels of 13.06% +/- 12.38% and 1.52% +/- 3.25% to 17.86% +/- 14.60% and 2.32% +/- 4.26% after 0.2 mT exposure and to 17.88% +/- 13.71% and 2.35% +/- 3.87% after 6.4 mT exposure (P < 0.05). Exposure to EMFs had not induced significant changes in S.D.alphaT and XalphaT, but COMPalphaT (cells outside the main population of alpha t), the percentage of sperms with abnormal chromatin structure, increased in the two exposed groups. CONCLUSION: 50 Hz EMFs may have the potential to induce DNA strand breakage in testicular cells and sperm chromatin condensation in mice.

(E)Hosseini E, Habibi MF, Babri S, Mohaddes G, Abkhezr H, Heydari H. Maternal stress induced anxiety-like behavior exacerbated by electromagnetic fields radiation in female rats offspring. PLoS One 17(8):e0273206, 2022.(BE, CE, IU, MO, VO)

There is a disagreement on whether extremely low frequency electromagnetic fields (ELF-EMF) have a beneficial or harmful effect on anxiety-like behavior. Prenatal stress induces frequent disturbances in offspring physiology such as anxiety-like behavior extending to adulthood. This study was designed to evaluate the effects of prenatal stress and ELF-EMF exposure before and during pregnancy on anxiety-like behavior and some anxiety-related pathways in the hippocampus of female rat offspring. A total of 24 female rats 40 days of age were distributed into four groups of 6 rats each: control, Stress (rats whose mothers underwent chronic stress), EMF (rats whose mothers were exposed to electromagnetic fields) and EMF/S (rats whose mothers were simultaneously exposed to chronic stress and ELF-EMF). The rats were given elevated plus-maze and open field tests and then their brains were dissected and their hippocampus were subjected to analysis. ELISA was used to measure 24(S)-hydroxy cholesterol, corticosterone, and serotonin levels. Cryptochrome2, steroidogenic acute regulatory protein, 3B-Hydroxy steroid dehydrogenase, N-methyl-D-aspartate receptor 2(NMDAr2) and phosphorylated N-methyl-D-aspartate receptor 2(PNMDAr2) were assayed by immunoblotting. Anxiety-like behavior increased in all treatment groups at the same time EMF increased anxiety induced by maternal stress in the EMF/S group. The stress group showed decreased serotonin and increased corticosterone levels. ELF-EMF elevated the PNMDAr2/NMDAr2 ratio and 24(S)-hydroxy cholesterol compared to the control group but did not change corticosterone. EMF did not restore changes induced by stress in behavioral and molecular tests. The results of the current study, clarified that ELF-EMF can induce anxiety-like behavior which may be attributed to an increase in the PNMDAr2/NMDAr2 ratio and 24(S)-OHC in the hippocampus, and prenatal stress may contribute to anxiety via a decrease in serotonin and an increase in corticosterone in the hippocampus. We also found that anxiety-like behavior induced by maternal stress exposure, is exacerbated by electromagnetic fields radiation.

(E)Hosseini E, Kianifard D. Effect of prenatal stress and extremely low-frequency electromagnetic fields on anxiety-like behavior in female rats: With an emphasis on prefrontal cortex and hippocampus. Brain Behav 13(4):e2949, 2023. (BE, CE, IU, IX, ME, MO, VO)

Objective: Prenatal stress (PS) is a problematic situation resulting in psychological implications such as social anxiety. Ubiquitous extremely low-frequency electromagnetic fields (ELF-EMF) have been confirmed as a potential physiological stressor; however, useful neuroregenerative effect of these types of electromagnetic fields has also frequently been reported. The aim of the present study was to survey the interaction of PS and ELF-EMF on anxiety-like behavior. Method: A total of 24 female rats 40 days of age were distributed into four groups of 6 rats each: control, stress (their mothers were exposed to stress), EMF (their mothers underwent to ELF-EMF), and EMF/stress (their mothers concurrently underwent to stress and ELF-EMF). The rats were assayed using elevated plus-maze and open field tests. Results: Expressions of the hippocampus GAP-43, BDNF, and caspase-3 (cas-3) were detected by immunohistochemistry in Cornu Ammonis 1 (CA1) and dentate gyrus (DG) of the hippocampus and prefrontal cortex (PFC). Anxiety-like behavior increased in all treatment groups. Rats in the EMF/stress group presented more serious anxiety-like behavior. In all treatment groups, upregulated expression of cas-3 was seen in PFC, DG, and CA1 and downregulated expression of BDNF and GAP-43 was seen in PFC and DG and the CA1. Histomorphological study showed vast neurodegenerative changes in the hippocampus and PFC. Conclusion: The results showed ,female rats that underwent PS or/and EMF exhibited critical anxiety-like behavior and this process may be attributed to neurodegeneration in PFC and DG of the hippocampus and possibly decreased synaptic plasticity so-called areas.

(NE) Huuskonen H, Juutilainen J, Komulainen H. Development of preimplantation mouse embryos after exposure to a 50 Hz magnetic field in vitro. Toxicol Lett 122(2):149-155, 2001. (CE, DE, IV)

Effect of sinusoidal 50 Hz magnetic field (MF) on development of preimplantation CBA/S mouse embryos in vitro was studied. Superovulated and in vivo fertilized preimplantation embryos were collected at one cell stage and divided to control and MF-exposed groups. Sinusoidal 50 Hz MF with field strength of 10 A/m r.m.s., corresponding a flux density of 13 microT r.m.s., was used to expose the embryos in culture at 37 degrees C in a CO2-incubator. The developmental stage and abnormalities were recorded twice daily except once daily during weekends. The vitality and developmental stages of the embryos were similar in both groups although slightly more dead embryos were found during the 1st day in MF-exposed group (P<0.05) and the development of MF-exposed embryos was slightly impaired. In conclusion, the exposure to sinusoidal 50 Hz MF at field strength of 10 A/m did not significantly disturb the development of the mouse embryos in vitro up to the blastocyst stage.

(E)Iorio R, Scrimaglio R, Rantucci E, Delle Monache S, Di Gaetano A, Finetti N, Francavilla F, Santucci R, Tettamanti E, Colonna R. A preliminary study of oscillating electromagnetic field effects on human spermatozoon motility. Bioelectromagnetics. 28(1):72-75, 2007. (AE, FC, IV, M) (wave-form dependent) Some effects of extremely low frequency electromagnetic fields (ELF-EMFs) on human spermatozoa are reported. Significant increases in the values of the motility and of the other kinematic parameters have been observed when spermatozoa were exposed to an ELF-EMF with a square waveform of 5 mT amplitude and frequency of 50 Hz. By contrast, a 5 mT sine wave (50 Hz) and a 2.5 mT square wave (50 Hz) exposure did not produce any significant effect on sperm motility. The effects induced by ELF-EMF (50 Hz; 5 mT) during the first 3 h of exposure persisted for 21 h after the end of the treatment. These results indicate that ELF-EMF exposure can improve spermatozoa motility and that this effect depends on the field characteristics.

(E)Iorio R, Delle Monache S, Bennato F, Di Bartolomeo C, Scrimaglio R, Cinque B, Colonna RC. Involvement of mitochondrial activity in mediating ELF-EMF stimulatory effect on human sperm motility. Bioelectromagnetics. 32(1):15-27, 2011. (AE, FC, IV, M, MO)

It has recently been reported that the exposure of human spermatozoa to an extremely low frequency (ELF) electromagnetic field (EMF) with a square waveform of 5 mT amplitude and frequency of 50 Hz improves sperm motility. The functional relationship between the energy metabolism and the enhancement of human sperm motility induced by ELF-EMF was investigated. Sperm exposure to ELF-EMF resulted in a progressive and significant increase of mitochondrial membrane potential and levels of ATP, ADP and NAD(+) that was associated with a progressive and significant increase in the sperm kinematic parameters. No significant effects were detected on other parameters such as ATP/ADP ratio and energy charge. When carbamoyl cyanide m-chlorophenylhydrazone (CICCP) was applied to inhibit the oxidative phosphorylation in the mitochondria, the values of energy parameters and motility in the sperm incubated in the presence of glucose and exposed to ELF-EMF did not change, thus indicating that the glycolysis was not involved in mediating ELF-EMF stimulatory effect on motility. By contrast, when pyruvate and lactate were provided instead of glucose, the energy status and motility increased significantly in ELF-EMF-treated sperm. Under these culture conditions, the inhibition of glycolitic metabolism by 2-deoxy-D-glucose (DOG) again resulted in increased values of energy and kinematic parameters, indicating that gluconeogenesis was not involved in producing glucose for use in glycolysis. We concluded that the key role in mediating the stimulatory effects exerted by ELF-EMF on human sperm motility is played by mitochondrial oxidative phosphorylation rather than glycolysis.

(NE) Ivanova DV, Ziganshin AU. Comparative Assessment of Disturbances of Contractions of the Isolated Uterus in 3- and 9-Month-Old Rats with a Model of Autism. Bull Exp Biol Med 175(3):341-344, 2023. (AE, F, FC, IV, electric field)

We performed a comparative study of the effects of carbachol, α , β -methylene-ATP, β , γ methylene-ATP, and electric field stimulation on the contractile activity of the isolated uterus from rats aged 3 and 9 months with valproic model of autism. The contractile responses of isolated rat uterine preparations induced by P2X-receptor agonists α , β -methylene-ATP and β , γ methylene-ATP were significantly lower than in the control. In addition, the contractions of the isolated uterus of 9-month-old rats induced by carbachol were significantly lower than in controls. No significant differences in uterine smooth muscle contractions in both age groups of rats induced by electric field stimulation in comparison with the control were found. Thus, significant impairment of uterine contractile activity was revealed in rats with valproic model of autism, which persisted up to the age of 9 months. <u>The absence of changes in the contractions induced by electric field stimulation suggests that the changes in the contractile activity of the uterus of the rats with modeled autism spectrum disorder are caused by the disorders occurring at the postsynaptic level.</u>

Jangid P, Rai U, Sharma RS, Singh R. The role of non-ionizing electromagnetic radiation on female fertility: A review. Int J Environ Health Res 33(4):358-373, 2023. (Review)

With increasing technological developments, exposure to non-ionizing radiations has become unavoidable as people cannot escape from electromagnetic field sources, such as Wi-Fi, electric wires, microwave oven, radio, telecommunication, bluetooth devices, etc. These radiations can be associated with increased health problems of the users. This review aims to determine the effects of non-ionizing electromagnetic radiations on female fertility. To date, several *in vitro* and *in vivo* studies unveiled that exposure to non-ionizing radiations brings about harmful effects on oocytes, ovarian follicles, endometrial tissue, estrous cycle, reproductive endocrine hormones, developing embryo, and fetal development in animal models. Non-ionizing radiation also upsurges the free radical load in the uterus and ovary, which leads to inhibition of cell growth and DNA disruptions. In conclusion, non-ionizing electromagnetic radiations can cause alterations in both germ cells as well as in their nourishing environment and also affect other female reproductive parameters that might lead to infertility.

(E) Juutilainen J, LääraE, Saali K. Relationship between field strength and abnormal development in chick embryos exposed to 50 Hz magnetic fields. Int J Radiat Biol Relat Stud Phys Chem Med 52(5):787-793, 1987. (AE, DE, IU) (1 A/m = 1.2μ)

Chick embryos were exposed to sinusoidally oscillating 50 Hz magnetic fields during their first 2 days of development. In the first series of experiments magnetic field strengths of 0.1, 0.3, 1 and 10 A/m were used. The percentage of abnormal embryos (% AE) was 16 per cent in the shamexposed control group. % AE was increased at 1 A/m (29 per cent) and 10 A/m (32 per cent), but not at 0.1 A/m (16 per cent) or 0.3 A/m (14 per cent). In the second series of experiments field strengths of 0.4, 0.6, 0.9 and 1.35 A/m were used. % AE was 17 per cent in the control group, 10 per cent at 0.4 A/m, 19 per cent at 0.6 A/m, 17 per cent at 0.9 A/m and 36 per cent at 1.35 A/m. Only the 1.35 A/m group was significantly different from the controls. The results of this study suggest that exposure of chick embryos to a 50 Hz magnetic field causes abnormal development, and that no abnormalities are induced below a threshold between 0.9 and 1 A/m.

(NE)Kale PG, Baum JW. Genetic effects of strong magnetic fields in Drosophila melanogaster: I. Homogeneous fields ranging from 13,000 to 37,000 Gauss. Environ Mutagen. 1(4):371-374, 1979. (CE, GE, IU, M)

Drosophila melanogaster males were exposed to homogeneous magnetic fields of intensities of 13,000 to 37,000 Gauss as eggs, larvae, pupae and as adults. Sex linked recessive lethals were scored in chromosomes exposed as spermatozoa, spermatids and as spermatocytes. There was no indication of enhanced mutation induction by the magnetic fields.

(NE)Kale PG, Baum JW. Genetic effects of strong magnetic fields in Drosophila melanogaster: II. lack of interaction between homogeneous fields and fission neutron-plus-gamma radiation. Environ Mutagen. 2(2):179-186, 1980. (CE, GE, M, VO)

Interaction between mutagenic effects of strong homogeneous magnetic fields and fission neutron-plus-gamma radiation was investigated, using the sex-linked, recessive, lethal test in Drosophila melanogaster. Drosophila males were exposed chronically, for seven days, to a 37,000-G homogeneous magnetic field and/or 3 doses of neutron-plus gamma radiation. Mutations in spermatozoa, spermatids, and spermatocytes were scored. There was no evidence of interaction between the effects of the two types of exposure in causing genetic damage in any of the three cell types. Dose-response relations for the radiation doses were linear for spermatozoa and spermatids for all three doses and for spermatocytes, up to 300 rads. Spermatozoa appear to be most sensitive to neutron-radiation-induced, recessive lethal mutations.

(E) Karbalay-

Doust S, Darabyan M, Sisakht M, Haddadi G, Sotoudeh N, Haghani M, Mortazavi SMJ Extremely Low Frequency-Electromagnetic Fields (ELF-EMF) Can Decrease Spermatocyte Count and Motility and Change Testicular Tissue. J Biomed Phys Eng 13(2):135-146, 2023. (CE, FC, M, ME, MO, VO)

Background: Substantial evidence indicates that exposure to extremely low frequencyelectromagnetic fields (ELF-EMFs) affects male reproductive system. Objective: The goal of this study was to evaluate the effects of long-term irradiation with ELF-EMF on sperm quality and quantity and testicular structure. Material and methods: In this case-control study, sixty male Sprague-Dawley rats were randomly divided into six groups. Experimental groups were exposed to ELF-EMF (50 Hz EMF, 100 µT) for either 1 h/day for 52 days (Group 1), 4 h/day for 52 days (Group 3), 1 h/day for 5 days (Group 5), 4 h/day for 52 days (Group 7). Groups 2, 4, 6 and 8 were only sham exposed at durations equal to Groups 1, 3, 5 and 7, respectively. **Results:** Both count and motility of sperms were significantly decreased in animals exposed to ELF-EMF (1 h/day for 52 days, 4 h/day for 52 day, and 4 h/day for 5 days) compared to the sham-exposed groups (P < 0.05). Serum testosterone levels showed a significant decrease in the animals exposed to ELF-EMF (4 h/day for 5 days) compared to the control groups (P<0.05). A significant decrease was observed in the volume of the seminiferous tubules, seminiferous tubules epithelium and interstitial tissue in the animals exposed to ELF-EMF for 4 h/day for 5 days. Tubules length was also reduced by 18% in animals exposed to ELF-EMF (4 h/day for 5 days). Conclusion: Our results show that ELF-EMF can reduce spermatocyte count and motility and is able to induce structural changes in testicular tissue.

(NE)Khan MW, Roivainen P, Herrala M, Tiikkaja M, Sallmén M, Hietanen M, Juutilain en J. A pilot study on the reproductive risks of maternal exposure to magnetic fields from electronic article surveillance systems. Int J Radiat Biol 94(10):902-908, 2018. (CE, F, HU)

Purpose: We investigated the feasibility of a large-scale epidemiological study on reproductive effects of intermediate frequency (IF) magnetic field (MF) exposure among cashiers working near electronic article surveillance (EAS) systems. **Materials and methods:** The study cohort

included 4157 women who had worked as cashiers in supermarkets with EAS devices (considered as exposed) or grocery stores without EAS devices (considered as unexposed) between 2008 and 2015. 536 births and 38 miscarriages occurred among these women during the study period, based on information from nationwide health registries. Measurements were also performed to characterize the MF exposure of cashiers. **Results:** Cashiers were found to be exposed to 8.2 MHz MFs only when passing by the gates at short distance. Static fields of about 0.1 mT were observed at cashier's seat. Extremely low frequency MFs were higher at stores without EAS devices. No differences on the risk of miscarriage, reduced birth weight or preterm birth were observed between cashiers in different store types. **Conclusions:** Any further studies should attempt to include study subjects working near EAS systems that produce stronger IF MFs at kHz frequencies. Exposure to ELF MFs should be assessed as a possible confounding factor.

(E)Kim H-S, Park B-J, Jang H-J, Ipper NS, Kim S-H, Kim Y-J, Jeon S-H, Lee K-S, Lee S-K, Kim N, Ju Y-J, Gimm Y-M, Kim Y-W. Continuous exposure to 60 Hz magnetic fields induces duration- and dose-dependent apoptosis of testicular germ cells. Bioelectromagnetics 35(2):100-107, 2014. (CE, M, ME, VO)

To evaluate duration- and dose-dependent effects of continuous exposure to a 60 Hz magnetic field (MF) on the testes in mice, BALB/c male mice were exposed to a 60 Hz MF at 100 μ T for 24 h a day for 2, 4, 6, or 8 weeks, and at 2, 20, or 200 μ T for 24 h a day for 8 weeks. Any exposures to MF did not significantly affect body or testicular masses. However, the apoptotic cells among testicular germ cells were increased duration-dependent at exposures of 100 μ T for 6 and 8 weeks and dose-dependent at exposures of 20 and 200 μ T for 8 weeks. The number of sperm in epididymis and the diameter of seminiferous tubule decreased in mice exposed to 100 and 200 μ T for 8 weeks, respectively. To induce the apoptosis of testicular germ cell in mice, the minimum dose is 20 μ T at continuous exposure to a 60 Hz MF for 8 weeks and the minimum duration is 6 weeks at continuous exposure of 100 μ T. Taken together, these results suggest that continuous exposure to a 60 Hz MF might affect, duration- and dose-dependent biological processes including apoptotic cell death and spermatogenesis in the male reproductive system of mice.

(E)Kim YW, Kim HS, Lee JS, Kim YJ, Lee SK, Seo JN, Jung KC, Kim N, Gimm YM. Effects of 60 Hz 14 microT magnetic field on the apoptosis of testicular germ cell in mice. Bioelectromagnetics. 30(1):66-67, 2009. (CE, M, ME, VO)

We recently reported that continuous exposure, for 8 weeks, of extremely low frequency (ELF) magnetic field (MF) of 0.1 or 0.5 mT might induce testicular germ cell apoptosis in BALB/c mice. In that report, the ELF MF exposure did not significantly affect the body weight or testicular weight, but significantly increased the incidence of testicular germ cell death. In the present study, we aimed to further characterize the effect of a 16-week continuous exposure to ELF MF of 14 or 200 microT on testicular germ cell apoptosis in mice. There were no significant effects of MF on body weight and testosterone levels in mice. In TUNEL staining (In situ terminal deoxynucleotidyl transferase-mediated deoxy-UTP nick end labeling), germ cells showed a significantly higher apoptotic rate in exposed mice than in sham controls (P < 0.001). TUNEL-positive cells were mainly spermatogonia. In an electron microscopic study,

degenerating spermatogonia showed condensation of nuclear chromatin similar to apoptosis. <u>These results indicate that apoptosis may be induced in spermatogenic cells in mice by</u> <u>continuous exposure to 60 Hz MF of 14 microT.</u>

(NE)Kowalczuk CI, Saunders RD. Dominant lethal studies in male mice after exposure to a 50-Hz electric field. Bioelectromagnetics. 11(2):129-137, 1990. (Parental exposure, Reproduction)

Male C3H/He mice were sham-exposed or exposed continuously for 2 weeks to a vertical, 50-Hz, electric field at 20 kV/m rms. Densities of currents induced in the testes are estimated to be near 100 microA/m2. After the exposure, each male was mated with two different female mice each week during a period of 8 weeks. By this schedule, female mice were impregnated with sperm that had been exposed to the electric field at different stages of the spermatogenic cycle. No significant differences as a function of exposure condition were observed in pregnancy rates or in survival of embryos before or after implantation. The absence of effects was not due to insensitivity of assays; other mice that were exposed to X-rays (dose to testes = 1.5 Gy) presented reliable evidence of mutagenesis.

(NE)Kowalczuk CI, Robbins L, Thomas JM, Saunders RD. Dominant lethal studies in male mice after exposure to a 50 Hz magnetic field. Mutat Res. 328(2):229-237, 1995. (Parental exposure, Reproduction)

The potential mutagenicity of power frequency magnetic fields was investigated using a dominant lethal assay in mice. A total of 42 male mice were exposed for 8 weeks to a 50 Hz sinusoidal magnetic field at 10 mT (rms) and 47 males acted as simultaneous cage controls. Each male was subsequently mated with two females on weeks 1, 3, 5, 7, and 9 post-exposure. The numbers of pregnant females, corpora lutea, and live and dead implants were recorded. Multiple logistic regression analyses examined the effects of exposure on pregnancy rate, pre-implantation survival and post-implantation survival. There were no statistically significant differences in overall response between exposed and control groups, nor was there any significant effect of exposure in any post-exposure week. <u>Thus, exposure to power frequency magnetic fields at 10 mT for the approximate period of spermatogenesis did not appear to induce dominant lethal mutation in the germ cells of male mice.</u>

(E)Koziorowska A, Depciuch J, Kozioł K, Nowak S, Lach K. In vitro study of effects of ELF-EMF on testicular tissues of roe deer (Capreolus capreolus) - FTIR and FT-Raman spectroscopic investigation. Anim Reprod Sci 213:106258, 2020. (AE, IV, M, MO)

Electromagnetic fields (EMF) are classified as an environmental factor affecting living organisms. The aim of the study was to evaluate the effect of EMF at different frequencies (50 and 120 Hz), durations of treatment (2 and 4 h) and with the magnetic induction of 8 m T on testicular tissues of roe deer (Capreolus capreolus) in vitro by comparison with the control samples. Fourier Transform Raman Spectroscopy (FT-Raman) and Fourier Transform Infrared Spectroscopy (FTIR) were utilized in this study to identify the chemical changes in the testicular

tissues. The FTIR and FT-Raman spectroscopy methods were used to evaluate differences in spectra of the treated tissues compared to the control group. The results from the analysis of the spectra indicated there were characteristic differences in the testicular tissue compared with the control samples. There was identification of peaks attributed to different biochemical components. Comparing the spectra for different frequencies and treatment times, there was a greater intensity of peaks originating from most of the functional groups in the tissues evaluated. With the FTIR spectra, there were five of 15 peaks, while with the FT-Raman spectra, there were six of ten peaks that were shifted. For FTIR and FT-Raman analyzed spectral ranges, results from the PCA analysis indicate there was no similarity between control groups (2 and 4 h) and samples treated with EMF at a frequency of 120 Hz for 2 and 4 h. In conclusion, therefore, EMF is an environmental factor affecting the testis of roe deer.

(E)Kozlowska W, Drzewiecka EM, Paukszto L, Zmijewska A, Wydorski PJ, Jastrzebski J P, Franczak A. Exposure to the electromagnetic field alters the transcriptomic profile in the porcine endometrium during the peri-implantation period. J Physiol Pharmacol 72(6), 2021. doi: 10.26402/jpp.2021.6.04. (AE, F, GE, IV)

A low-frequency electromagnetic field (EMF) is an environmental pollutant that may influence female reproduction. This research was undertaken to test the hypothesis that EMF causes alterations in the transcriptomic profile of the endometrium. This study investigated the in vitro effects of EMF treatment (50 Hz, 2 h) on global transcriptome alterations in the endometrium isolated from pigs during the peri-implantation period. The control endometrium was not treated with EMF. The EMF treatment altered the expression of 1561 transcriptionally active regions (TARs) in the endometrium. In the group of 461 evaluated DEGs, 156 were up-regulated (34%), 305 were down-regulated (66%) and 341 (74%) had known biological functions. A total of 210 long noncoding RNAs (lncRNAs) with changes in expression profiles, and 146 predicted RNA editing sites were also evaluated. Exposure to EMF changes the expression of genes encoding proteins that are involved in proliferation and metabolism in endometrial tissue. These results provide useful inputs for further research into the impact of EMF on molecular changes in the uterus during the peri-implantation period and, consequently, pregnancy outcome.

(E)Lee JS, Ahn SS, Jung KC, Kim YW, Lee SK. Effects of 60 Hz electromagnetic field exposure on testicular germ cell apoptosis in mice. Asian J Androl. 6(1):29-34, 2004. (CE, M, ME, VO)

AIM: To evaluate the effects of 60 Hz extremely low frequency (ELF) electromagnetic field (EMF) exposure on germ cell apoptosis in the testis of mice. METHODS: Adult male BALB/c mice (7 weeks of age) were exposed to a 60 Hz EMF of 0.1 mT or 0.5 mT for 24 h/day. A sham-exposed group served as the control. After 8 weeks of exposure, the mice were sacrificed. Germ cell apoptosis in the testis was assessed by histopathological examination, the terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling assay (TUNEL) and flow cytometric examination of isolated spermatogenic cells stained with 7 aminoactinomycin D (7-AAD). RESULTS: EMF exposure did not significantly affect the body and testis weights, but significantly increased the incidence of germ cell death. The distinguishing morphological feature of EMF exposure was a decrement in the number of well organized seminiferous tubules. Quantitative analysis of TUNEL-positive germ cells showed a significantly higher apoptotic rate

in the 0.5 mT exposed mice than that in the sham controls (P<0.05), while the difference between the two exposed groups was insignificant. The TUNEL-positive cells were mainly spermatogonia. In flow cytometry analysis, the percentage of live cells [forward scatter count (FSC)(high)7-AAD(-)] was lower in the exposed groups than that in the controls (Figure 5A), but the decrease in viability was not statistically significant. CONCLUSION: <u>Continuous exposure to ELF EMF may induce testicular germ cell apoptosis in mice.</u>

Lee S-K, Park S, Gimm Y-M, Kim Y-W. Extremely low frequency magnetic fields induce spermatogenic germ cell apoptosis: possible mechanism. Biomed Res Int 2014:567183, 2014. (Review)

The energy generated by an extremely low frequency electromagnetic field (ELF-EMF) is too weak to directly induce genotoxicity. However, it is reported that an extremely low frequency magnetic field (ELF-MF) is related to DNA strand breakage and apoptosis. The testes that conduct spermatogenesis through a dynamic cellular process involving meiosis and mitosis seem vulnerable to external stress such as heat, MF exposure, and chemical or physical agents. Nevertheless the results regarding adverse effects of ELF-EMF on human or animal reproductive functions are inconclusive. According to the guideline of the International Commission on Non-Ionizing Radiation Protection (ICNIRP; 2010) for limiting exposure to time-varying MF (1 Hz to 100 kHz), overall conclusion of epidemiologic studies has not consistently shown an association between human adverse reproductive outcomes and maternal or paternal exposure to low frequency fields. In animal studies there is no compelling evidence of causal relationship between prenatal development and ELF-MF exposure. However there is increasing evidence that EL-EMF exposure is involved with germ cell apoptosis in testes. Biophysical mechanism by which ELF-MF induces germ cell apoptosis has not been established. This review proposes the possible mechanism of germ cell apoptosis in testes induced by ELF-MF.

(E)Li DK, Yan B, Li Z, Gao E, Miao M, Gong D, Weng X, Ferber JR, Yuan W. Exposure to magnetic fields and the risk of poor sperm quality. Reprod Toxicol. 29(1):86-92, 2010. (CE, FC, HU, M, ME)

We conducted a population-based case-control study among healthy sperm donors to study exposure to magnetic fields (MFs) and poor sperm quality. All participants wore a meter to capture daily MF exposure. After controlling for confounders, compared to those with lower MF exposure, those whose 90th percentile MF level > or = 1.6 mG had a two-fold increased risk of abnormal sperm motility and morphology (odds ratio (OR): 2.0, 95% confidence interval (CI): 1.0-3.9). Increasing duration of MF exposure above 1.6 mG further increased the risk (p=0.03 for trend test). Importantly, the association and dose-response relationship were strengthened when restricted to those whose measurement day reflected their typical day of the previous 3 months (a likely period of spermatogenesis). Age-adjusted Spearman Rank Order Correlations showed an inverse correlation between MF exposure and all semen parameters. <u>Our study provides some</u> evidence for the first time that MF exposure may have an adverse effect on sperm quality.

(E) Li S-S, Zhang Z-Y, Yang C-J, Lian H-Y, Cai P. Gene expression and reproductive abilities of male Drosophila melanogaster subjected to ELF-EMF exposure. Mutat Res Genet Toxicol Environ Mutagen 758(1-2):95-103, 2013. (AE, GE, M, VO)

Extremely low frequency electromagnetic field (ELF-EMF) exposure is attracting increased attention as a possible disease-inducing factor. The in vivo effects of short-term and long-term ELF-EMF exposure on male Drosophila melanogaster were studied using transcriptomic analysis for preliminary screening and QRT-PCR for further verification. Transcriptomic analysis indicated that 439 genes were up-regulated and 874 genes were down-regulated following shortterm exposures and that 514 genes were up-regulated and 1206 genes were down-regulated following long-term exposures (expression >2- or <0.5-fold, respectively). In addition, there are 238 up-regulated genes and 598 down-regulated genes in the intersection of short-term and longterm exposure (expression >2- or <0.5-fold). The DEGs (differentially expressed genes) in D. melanogaster following short-term exposures were involved in metabolic processes, cytoskeletal organization, mitotic spindle organization, cell death, protein modification and proteolysis. Long-term exposure let to changes in expression of genes involved in metabolic processes, response to stress, mitotic spindle organization, aging, cell death and cellular respiration. In the intersection of short-term and long-term exposure, a series of DEGs were related to apoptosis, aging, immunological stress and reproduction. To check the ELF-EMF effects on reproduction, some experiments on male reproduction ability were performed. Their results indicated that short-term ELF-EMF exposure may decrease the reproductive ability of males, but long-term exposures had no effect on reproductive ability. Down-regulation of ark gene in the exposed males suggests that the decrease in reproductive capacity may be induced by the effects of ELF-EMF exposure on spermatogenesis through the caspase pathway. QRT-PCR analysis confirmed that jra, ark and decay genes were down regulated in males exposed for 1 Generation (1G) and 72 h, which suggests that apoptosis may be inhibited in vivo. ELF-EMF exposure may have accelerated cell senescence, as suggested by the down-regulation of both cat and jra genes and the up-regulation of hsp22 gene. Up-regulation of totA and hsp22 genes during exposure suggests that exposed flies might induce an in vivo immune response to counter the adverse effects encountered during ELF-EMF exposure. Down-regulation of cat genes suggests that the partial oxidative protection system might be restrained, especially during short-term exposures. This study demonstrates the bioeffects of ELF-EMF exposure and provides evidence for understanding the in vivo mechanisms of ELF-EMF exposure on male D. melanogaster.

Liorni I, Parazzini M, Fiocchi S, Ravazzani P. Exposure of high resolution fetuses in advanced pregnant woman models at different stages of pregnancy to uniform magnetic fields at the frequency of 50 Hz. Annu Int Conf IEEE Eng Med Biol Soc 2013:4525-4528, 2013. (Dosimetry)

Extremely low frequency magnetic fields (ELF-MF) have been considered as a possible risk factor for childhood leukemia by several epidemiological studies. In this work the exposure assessment of fetuses at 3, 7 and 9 months of Gestational Age (GA) to differently polarized uniform magnetic fields at the frequency of 50 Hz by means of high resolution numerical models of pregnant women is carried out. This set of models is used to analyze the fetal tissue-specific induced electric fields and current densities as a function of both the incident magnetic field polarization and the GA.

Liorni I, Parazzini M, Fiocchi S, Ravazzani P. Study of the influence of the orientation of a 50-Hz magnetic field on fetal exposure using polynomial chaos decomposition. Int J Environ Res Public Health 12(6):5934-5953, 2015. (Dosimetry)

Human exposure modelling is a complex topic, because in a realistic exposure scenario, several parameters (e.g., the source, the orientation of incident fields, the morphology of subjects) vary and influence the dose. Deterministic dosimetry, so far used to analyze human exposure to electromagnetic fields (EMF), is highly time consuming if the previously-mentioned variations are considered. Stochastic dosimetry is an alternative method to build analytical approximations of exposure at a lower computational cost. In this study, it was used to assess the influence of magnetic flux density (B) orientation on fetal exposure at 50 Hz by polynomial chaos (PC). A PC expansion of induced electric field (E) in each fetal tissue at different gestational ages (GA) was built as a function of B orientation. Maximum E in each fetal tissue and at each GA was estimated for different exposure configurations and compared with the limits of the International Commission of Non-Ionising Radiation Protection (ICNIRP) Guidelines 2010. PC theory resulted in an efficient tool to build accurate approximations of E in each fetal tissue. B orientation strongly influenced E, with a variability across tissues from 10% to 43% with respect to the mean value. However, varying B orientation, maximum E in each fetal tissue was below the limits of ICNIRP 2010 at all GAs.

Liorni I, Parazzini M, Fiocchi S, Douglas M, Capstick M, Kuster N, Ravazzani P. COMPUTATIONAL ASSESSMENT OF PREGNANT WOMAN MODELS EXPOSED TO UNIFORM ELF-MAGNETIC FIELDS: COMPLIANCE WITH THE EUROPEAN CURRENT EXPOSURE REGULATIONS FOR THE GENERAL PUBLIC AND OCCUPATIONAL EXPOSURES AT 50 Hz. Radiat Prot Dosimetry 172(4):382-392, 2016. (Dosimetry)

The Recommendation 1999/529/EU and the Directive 2013/35/EU suggest limits for both general public and occupational exposures to extremely low-frequency magnetic fields, but without special limits for pregnant women. This study aimed to assess the compliance of pregnant women to the current regulations, when exposed to uniform MF at 50 Hz (100 μ T for EU Recommendation and 1 and 6 mT for EU Directive). For general public, exposure of pregnant women and fetus always resulted in compliance with EU Recommendation. For occupational exposures, (1) Electric fields in pregnant women were in compliance with the Directive, with exposure variations due to fetal posture of <10 %, (2) electric fields in fetuses are lower than the occupational limits, with exposure variations due to fetal posture of >40 % in head tissues, (3) Electric fields in fetal CNS tissues of head are above the ICNIRP 2010 limits for general public at 1 mT (in 7 and 9 months gestational age) and at 6 mT (in all gestational ages).

(E)Liu Y, Liu WB, Liu KJ, Ao L, Zhong JL, Cao J, Liu JY. Effect of 50 Hz extremely lowfrequency electromagnetic fields on the DNA methylation and DNA methyltransferases in mouse spermatocyte-derived cell line GC-2. Biomed Res Int. 2015:237183, 2015. (AE, GE, IV, M)

Previous studies have shown that the male reproductive system is one of the most sensitive organs to electromagnetic radiation. However, the biological effects and molecular mechanism are largely unclear. Our study was designed to elucidate the epigenetic effects of 50 Hz ELF-EMF in vitro. Mouse spermatocyte-derived GC-2 cell line was exposed to 50 Hz ELF-EMF (5 min on and 10 min off) at magnetic field intensity of 1 mT, 2 mT, and 3 mT with an intermittent exposure for 72 h. We found that 50 Hz ELF-EMF exposure decreased genome-wide

methylation at 1 mT, but global methylation was higher at 3 mT compared with the controls. The expression of DNMT1 and DNMT3b was decreased at 1 mT, and 50 Hz ELF-EMF can increase the expression of DNMT1 and DNMT3b of GC-2 cells at 3 mT. However, 50 Hz ELF-EMF had little influence on the expression of DNMT3a. Then, we established DNA methylation and gene expression profiling and validated some genes with aberrant DNA methylation and expression at different intensity of 50 Hz ELF-EMF. These results suggest that the alterations of genome-wide methylation and DNMTs expression may play an important role in the biological effects of 50 Hz ELF-EMF exposure.

(E)Liu Y, Liu W-B, Liu K-J, Ao L, Cao J, Zhong JL, Liu J-Y. Extremely Low-Frequency Electromagnetic Fields Affect the miRNA-Mediated Regulation of Signaling Pathways in the GC-2 Cell Line. PLoS One10(10):e0139949, 2015. (AE, GE, IV, M)

Extremely low-frequency electromagnetic fields (ELF-EMFs) can affect male reproductive function, but the underlying mechanism of this effect remains unknown. miRNA-mediated regulation has been implicated as an important epigenetic mechanism for regulatory pathways. Herein, we profiled miRNA expression in response to ELF-EMFs in vitro. Mouse spermatocytederived GC-2 cells were intermittently exposed to a 50 Hz ELF-EMF for 72 h (5 min on/10 min off) at magnetic field intensities of 1 mT, 2 mT and 3 mT. Cell viability was assessed using the CCK-8 assay. Apoptosis and the cell cycle were analyzed with flow cytometry. miRNA expression was profiled using Affymetrix Mouse Genechip miRNA 3.0 arrays. Our data showed that the growth, apoptosis or cell cycle arrest of GC-2 cells exposed to the 50 Hz ELF-EMF did not significantly change. However, we identified a total of 55 miRNAs whose expression significantly changed compared with the sham group, including 19 differentially expressed miRNAs (7 miRNAs were upregulated, and 12 were downregulated) in the 1 mT exposure group and 36 (9 miRNAs were upregulated, and 27 were downregulated) in the 3 mT exposure group. The changes in the expression of 15 selected miRNAs measured by real-time PCR were consistent with the microarray results. A network analysis was used to predict core miRNAs and target genes, including miR-30e-5p, miR-210-5p, miR-196b-5p, miR-504-3p, miR-669c-5p and miR-455-3p. We found that these miRNAs were differentially expressed in response to different magnetic field intensities of ELF-EMFs. GO term and KEGG pathway annotation based on the miRNA expression profiling results showed that miRNAs may regulate circadian rhythms, cytokine-cytokine receptor interactions and the p53 signaling pathway. These results suggested that miRNAs could serve as potential biomarkers, and the miRNA-mediated regulation of signaling pathways might play significant roles in the biological effects of ELF-EMFs.

(E)Liu Y, Liu W-B, Liu K-J, Ao L, Cao J, Zhong JL, Liu J-Y. Overexpression of miR-26b-5p regulates the cell cycle by targeting CCND2 in GC-2 cells under exposure to extremely low frequency electromagnetic fields. Cell Cycle 15(3):357-367, 2016. (AE, GE, IV, M)

The increasing prevalence of extremely low frequency electromagnetic fields (ELF-EMFs) exposure has raised considerable public concern regarding the potential hazardous effects of ELF-EMFs on male reproductive function. Increasing evidence indicates that miRNAs are necessary for spermatogenesis and male fertility. However, the regulation of miRNA expression and the roles of miRNAs in response to ELF-EMFs remain unclear. In our study, mouse spermatocyte-derived GC-2 cells were intermittently exposed to a 50 Hz ELF-EMF for 72 h (5

min on/10 min off) at magnetic field intensities of 1 mT, 2 mT and 3 mT. MiR-26b-5p was differentially expressed in response to different magnetic field intensities of ELF-EMFs. The host gene CTDSP1 showed an unmethylation status in GC-2 cells at different magnetic field intensities of ELF-EMF exposure. MiR-26b-5p had no significant, obvious influence on the cell viability, apoptosis or cell cycle of GC-2 cells. However, the overexpression of miR-26b-5p significantly decreased the percentage of G0/G1 phase cells and slightly increased the percentage of S phase cells compared to the sham group that was exposed to a 50 Hz ELF-EMF. Computational algorithms identified Cyclin D2 (CCND2) as a direct target of miR-26b-5p. MiR-26b-5p and a 50 Hz ELF-EMF altered the expression of CCND2 at both the mRNA and protein levels. Overexpressed miR-26b-5p in GC-2 cells can change the mRNA expression of CCND2 following 50 Hz ELF-EMF at 3 mT. These findings demonstrate that miR-26b-5p could serve as a potential biomarker following 50 Hz ELF-EMF exposure, and miR-26b-5p-CCND2-mediated cell cycle regulation might play a pivotal role in the biological effects of ELF-EMFs.

(NE)Lundsberg LS, Bracken MB, Belanger K. Occupationally related magnetic field exposure and male subfertility. Fertil Steril. 63(2):384-391, 1995. (CE, HU, M, ME)

OBJECTIVE: To determine whether there is an association between occupationally related magnetic field exposure, as estimated in milligauss (mG), and male subfertility. DESIGN: Nested case-control study using three defined case groups and one standard control group. SETTING: Yale New Haven Hospital Infertility Clinic, New Haven, Connecticut. PATIENTS, INTERVENTIONS: Male partners of couples seeking diagnosis and care at the infertility clinic. Men included in the analysis had complete first semen analysis and interview information. Subjects for this investigation consisted of case groups for motility (n = 177), morphology (n =135), and concentration (n = 172); controls included men normal on all three parameters (n = 172); 304). MAIN OUTCOME MEASURES: Laboratory confirmation in semen analysis of poor morphology, inadequate motility, and low concentration. Comparisons of occupational magnetic field exposure categories are made between case groups and controls. RESULTS: The odds of high job exposure category to magnetic fields (> 3 mG [> 0.3 muT]) for morphology cases were odds ratio (OR) = 0.6, for motility cases OR = 1.1, and concentration cases OR = 1.0 as compared with controls. No significant association was demonstrated for medium exposure (> 2 to 3 mG) among all case groups. Multivariate adjustment for selected risk factors did not substantially change estimates of risk. CONCLUSIONS: A lack of association between occupationally related categories of magnetic field exposure and male subfertility, as evaluated by morphology, motility, and concentration, has been demonstrated. These findings do not substantiate theories of deleterious effects to male reproductive health from magnetic fields.

(E)Mahmoudabadi FS, Ziaei S, Firoozabadi M, Kazemnejad A. Exposure to extremely low frequency electromagnetic fields during pregnancy and the risk of spontaneous abortion: a case-control study. J Res Health Sci 13(2):131-134, 2013. (CE, F, FC, HU)

Background: Exposure to extremely low frequency electromagnetic fields is increasingly common, but the potential influence on pregnant women has not been thoroughly investigated. **Methods:** In this case-control study, 58 women who had an unexplained spontaneous abortion at < 14 weeks gestation and 58 matched pregnant women >14 weeks gestation were enrolled in 2012. The women completed the questionnaire, which was used to collect data about

socioeconomic and obstetric characteristics, medical and reproductive histories. Then, to evaluate the extremely low frequency electromagnetic fields , we determined the magnitude of electromagnetic fields in the participants' houses by an exposure level tester (3D EMF tester/ Model: ELF-828; Taiwan). The instrument covers a limited frequency range (30 HZ to 3 KHZ). **Results:** The magnitude of extremely low frequency electromagnetic fields in the participants' houses was significantly different between the two groups (P<0.001). **Conclusions:** Extremely low frequency electromagnetic fields exposure is probably related to early spontaneous abortions.

(NE)Migault L, Piel C, Carles C, Delva F, Lacourt A, Cardis E, Zaros C, de Seze R, Baldi I, Bouvier G. Maternal cumulative exposure to extremely low frequency electromagnetic fields and pregnancy outcomes in the Elfe cohort. Environ Int 112:165-173, 2018. (CE, DE, HU, IU)

Objectives: To study the relations between maternal cumulative exposure to extremely low frequency electromagnetic fields (ELF EMF) and the risk of moderate prematurity and small for gestational age within the Elfe cohort. Methods: The Elfe study included 18,329 infants born at 33weeks of gestation or more in France in 2011 and was designed to follow the children until 20 years of age. Gestational age and anthropometric data at birth were collected in medical records and small for gestational age was defined according to a French customized growth standard. During interviews, mothers were asked to report their job status during pregnancy. If employed, their occupation was coded according to the International Standard Classification of Occupations 1988 and the date on which they stopped their work was recorded. Cumulative exposure to ELF EMF during pregnancy was assessed, for both mothers who worked and those who did not during pregnancy, using a recently-updated job-exposure matrix (JEM). Cumulative exposure was considered as a categorical variable (<17.5, 17.5-23.8, 23.8-36.2, 36.2-61.6 or ≥61.6µTdays), a binary variable (<44.1 and \geq 44.1µT-days) and a continuous variable. Associations were analyzed by logistic regression, adjusting for the mother's lifestyle factors, sociodemographic characteristics and some mother's medical history during and before pregnancy. Analyses were restricted to single births and to complete values for the pregnancy outcomes (n=16,733). **Results:** Cumulative exposure was obtained for 96.0% of the mothers. Among them, 37.5% were classified in the 23.8-36.2µT-days category, but high exposures were rare: 1.3% in the \geq 61.6µT-days category and 5.5% in the \geq 44.1µT-days category. No significant association was observed between maternal cumulative exposure and moderate prematurity and small for gestational age in this exposure range. Conclusion: This large population-based study does not suggest that maternal exposure to ELF EMF during pregnancy is highly associated with risks of moderate prematurity or small for gestational age.

(NE)Migault L, Garlantézec R, Piel C, Marchand-

Martin L, Orazio S, Cheminat M, Zaros C, Camille Carles C, Cardis E, Ancel P-Y, M-A, de Seze R, Baldi I, Bouvier G. Maternal cumulative exposure to extremely low frequency electromagnetic fields, prematurity and small for gestational age: a pooled analysis of two birth cohorts. Occup Environ Med 77(1):22-31, 2020. (CE, DE, HU, IU)

Background: Data on the effects of extremely low frequency electromagnetic fields (ELF-EMF) on pregnancy outcomes are inconclusive. **Objective:** To study the relation between maternal

cumulative exposure to ELF-EMF during pregnancy and the risk of prematurity or small for gestational age (SGA) in a pooled analysis of two French birth cohorts. Methods: Elfe and Epipage2 are both population-based birth cohorts initiated in 2011 and included 18 329 and 8400 births, respectively. Health data and household, mother and child characteristics were obtained from medical records and questionnaires at maternity and during follow-up. A job exposure matrix was used to assess cumulative exposure to ELF-EMF during three periods: (1) until 15 weeks of gestation, (2) until 28 weeks of gestation and (3) until 32 weeks of gestation. Analyses were restricted to single live births in mainland France and to mothers with documented jobs (N=19 894). Adjusted logistic regression models were used. Results: According to the period studied, 3.2%-4% of mothers were classified as highly exposed. Results were heterogeneous. Increased risks of prematurity were found among low exposed mothers for the three periods, and no association was observed among the most exposed (OR1=0.92 (95% CI 0.74 to 1.15); OR2=0.98 (95% CI 0.80 to 1.21); OR3=1.14 (95% CI 0.92 to 1.41)). For SGA, no association was observed with the exception of increased risk among the low exposed mothers in period 2 and the most exposed in period 3 (OR=1.25 (95% CI 1.02 to 1.53)). Conclusion: Some heterogeneous associations between ELF-EMF exposure and prematurity and SGA were observed. However, due to heterogeneity (ie, their independence regarding the level of exposure), associations cannot be definitely explained by ELF-EMF exposure.

Milan HFM, Almazloum AA, Bassani RA, Bassani JWM. Membrane polarization at the excitation threshold induced by external electric fields in cardiomyocytes of rats at different developmental stages. Med Biol Eng Comput 61(10):2637-2647, 2023. (Dosimetry)

External electric fields (E), used for cardiac pacing and defibrillation/cardioversion, induce a spatially variable change in cardiomyocyte transmembrane potential (Δ Vm) that depends on cell geometry and E orientation. This study investigates E-induced Δ Vm in cardiomyocytes from rats at different ages, which show marked size/geometry variation. Using a tridimensional numerical electromagnetic model recently proposed (NM3D), it was possible: (a) to evaluate the suitability of the simpler, prolate spheroid analytical model (PSAM) to calculate amplitude and location of Δ Vm maximum (Δ Vmax) for E = 1 V.cm-1; and (b) to estimate the Δ Vmax required for excitation (Δ VT) from experimentally determined threshold E values (ET). Ventricular myocytes were isolated from neonatal, weaning, adult, and aging Wistar rats. NM3D was constructed as the extruded 2D microscopy cell image, while measured minor and major cell dimensions were used for PSAM. Acceptable Δ Vm estimates can be obtained with PSAM from paralelepidal cells for small θ . ET, but not Δ VT, was higher for neonate cells. Δ VT was significantly greater in the cell from older animals, which indicate lower responsiveness to E associated with aging, rather than with altered cell geometry/dimensions. Δ VT might be used as a non-invasive indicator of cell excitability as it is little affected by cell geometry/size.

(E)Milan PB, Nejad DM, Ghanbari AA, Rad JS, Nasrabadi HT, Roudkenar MH, Roushandeh AM, Goldust M. Effects of Polygonum aviculare herbal extract on sperm parameters after EMF exposure in mouse. Pak J Biol Sci. 14(13):720-724, 2011.(CE, FC, M, VO)

Electromagnetic fields with high energy same as ionizing radiation inserts their destructive effects via free radical production. Using antioxidants or herbal plants with antioxidants

components could diminish hazardous effects of EMF. Polygonum aviculare has a high amount of phenolic and flavonoid and proved that has antioxidants effects. The aim of this study was to evaluate the effects of Polygonum aviculare herbal extract on sperm parameters after EMF exposure in mouse. Twenty four male mice, 8 weeks divided to 4 groups (one control and three experimental groups). Control group didn't receive EMF exposure. EMF group mice received 3 mT EMF during 2 months, 4 h daily and 5 days weekly. Polygonum aviculare group received 50 mg kg(-1) herbal extract during 2 months and poly -EMF group received 3 mT EMF during 2 months, 4 h daily and 50 mg kg(-1) herbal extract during 2 months. After 2 months the mice sacrificed with cervical dislocation and sperm obtained from tail of epididymis and motility and morphology of them were analyzed. Sperm analysis results showed that in group with Polygonum aviculare, morphology and motility of sperm developed (p < 0.05). Present results showed that EMF can reduce motility of sperm and treatment of Polygonum aviculare after EMF exposure developed sperm quality after EMF exposure.

(E)Monfared AS, Jorsaraei SG, Abdi R. Protective effects of vitamins C and E on spermatogenesis of 1.5 Tesla magnetic field exposed rats. J Magn Reson Imaging. 30(5):1047-1051, 2009. (AE, M, ME, OX, VO)

PURPOSE: To investigate protective effects of vitamins E and C against 1.5 Tesla static magnetic fields in magnetic resonance imaging (MRI) on spermatogenesis parameters was the main goal of the present study. MATERIALS AND METHODS: Ninety-two mature male rats were exposed to 1.5 T MRI static magnetic fields for 30 min with or without vitamins C and E alone or in combination. Animals were sacrificed and the testicular tissues were anatomically sectioned, stained, and the number of germ cells and the diameters of sperm ducts were measured and compared with sham and controls. RESULTS: Results showed that compared to sham, static magnetic fields may reduce the germ cell count (P = 0.000) and sperm ducts diameters (P = 0.020), and vitamins C and E could modify the reduction in germ cell count (P = 0.019) but they did not show any protective effect on sperm duct diameter reduction (0.647). CONCLUSION: The protective effects of vitamins C and E are different, and depend on the type of effects. It seems that the modifying effects of vitamins are to be additive, but vitamin E plays a more important role than vitamin C against the static magnetic field on spermatogenesis parameters in clinical MRI.

(E)Muti ND, Salvio G, Ciarloni A, Perrone M, Tossetta G, Lazzarini R, Bracci M, Balerci a G. Can extremely low frequency magnetic field affect human sperm parameters and male fertility? Tissue Cell 82:102045, 2023. (AE, FC, M, ME, OX, VO)

Exposure to extremely low frequency magnetic fields (ELF-MF) may have different effects on spermatozoa depending on the waveform, magnetic flux density, frequency of ELF-MF, and duration of exposure. In this study, we investigated the possible role of ELF-MF (50 Hz; 1 mT) exposure in altering sperm parameters. In this study we found that exposure to ELF-MF at the frequency of 50 Hz (1 mT) for two hours induces statistically significant alterations in progressive motility, morphology and reactive oxygen species (ROS) production of human spermatozoa, suggesting a role of ELF-MF in altering reproductive function of spermatozoa. Our

results represent an important discovery in the field since occupational exposure to the sine waveform 1 mT 50 Hz ELF-MF used in our study is possible in workplace. Moreover, these electromagnetic fields are product by many electronic devices and household appliances. Thus, alterations of progressive motility and morphology of spermatozoa would be important consequences of human exposures to ELF-MF.

(E)Narra VR, Howell RW, Goddu SM, Rao DV. Effects of a 1.5-Tesla static magnetic field on spermatogenesis and embryogenesis in mice. Invest Radiol. 31(9):586-590, 1996. (AE, DE, IV, M, ME)

RATIONALE AND OBJECTIVES: There is a trend toward the use of higher magnetic field strengths in magnetic resonance imaging procedures. Considering this trend and the lack of consensus on the biologic effects of static magnetic fields, it is of considerable interest to examine the biologic effects of a 1.5-tesla (T) static magnetic field on spermatogenesis and embryogenesis in mice. METHODS: Male and pregnant female Swiss Webster mice were exposed to a 1.5-T static magnetic field for 30 minutes. Effects on spermatogenesis in male mice were investigated by counting testicular spermheads and epididymal spermhead shapeabnormalities as a function of time after exposure. Pregnant female mice were exposed to the field at the two-cell embryo stage, sacrificed immediately, and the ability of these preimplantation embryos to mature into blastocysts was examined in vitro. RESULTS: Exposure to the static 1.5-T magnetic field caused a statistically significant reduction (15%) in testicular sperm on the 16th and 29th days after exposure. However, the increase in spermhead shape abnormalities above normal control values was minimal. A substantial effect was noted on the development of preimplantation embryos with a survival fraction of 0.56 compared with controls. CONCLUSIONS: A 30-minute exposure to a 1.5-T static magnetic field appears to cause some deleterious effects on spermatogenesis and embryogenesis in mice.

(E)Oliva M, De Marchi L, Cuccaro A, Fumagalli G, Freitas R, Fontana N, Raugi M, Barmada S, Pretti C. Introducing energy into marine environments: A lab-scale static magnetic field submarine cable simulation and its effects on sperm and larval development on a reef forming serpulid. Environ Pollut. 328:121625, 2023. (AE, GE, IV, M, MO, OX)

Non-chemical sources of anthropogenic environmental stress, such as artificial lights, noise and magnetic fields, are still an underestimate factor that may affect the wildlife. Marine environments are constantly subjected to these kinds of stress, especially nearby to urbanized coastal areas. In the present work, the effect of static magnetic fields, associated with submerged electric cables, was evaluated in gametes and early life stages of a serpulid polychaete, namely Ficopomatus enigmaticus. Specifically, biochemical/physiological impairments of sperm, fertilization rate inhibition and incorrect larval development were assessed. We evaluated differences between two selected magnetic field induction values (0.5 and 1 mT) along a range of exposure times (30 min-48 h), for a sound evaluation on this species. We found that a magnetic induction of 1 mT, a typical value that can be found at distance of tens of cm from a submerged cable, may be considered a biologically and ecologically relevant for sessile organisms and for coastal environments more generally. This value exerted statistically significant effects on membranes, DNA integrity, kinetic parameters and mitochondrial activity of sperm cells. Moreover, a significant reduction in fertilization rate was observed in sperm

exposed to the same magnetic induction level (1 mT) for 3 h, compared to controls. Regarding early larval stages, 48-h exposure did not affect the correct development. Our results represent a starting point for a future focus of research on magnetic field effects on early life stages of aquatic invertebrates, using model species as representative for reef-forming/encrusting organisms and ecological indicators of soft sediment quality.

Otto M, von Mühlendahl KE. Electromagnetic fields (EMF): do they play a role in children's environmental health (CEH)? Int J Hyg Environ Health 210(5):635-644, 2007. (Review)

Possible adverse health effects of exposure to electric, magnetic and electromagnetic fields (EMF), and especially the question of whether there exists a special vulnerability of children, have been a much discussed topic during the last two decades. Static fields produce health effects only in very rare and exceptional circumstances at extremely high field intensities. As for lowfrequency EMF, the results of epidemiological research with respect to childhood leukaemia prompted the International Agency for Research on Cancer (IARC) in 2001 to classify these fields as "possibly carcinogenic to humans". Current hypotheses on the mechanism of such action are presented. The effect, if existent, appears to be not very important in relation to established other causes of childhood leukaemia. High-frequency EMF, as used in mobile and wireless communication (mobile telephony according to the GSM and UMTS standard, cordless DECT phones, wireless local area networks (WLAN), Bluetooth) and since many decades also in radio and television technology, are practically omnipresent. At high intensities, the generation of heat is the principal effect. Current guidelines, limits and regulations prevent any such effect. Mobile phone calls may, in certain circumstances, lead to local exposures close to limit values. Base stations typically produce exposures lower by 2-5 magnitudes. The discussion centres on the so-called non-thermal effects, which are supposedly occurring at field intensities, which are by orders of magnitude lower than those responsible for thermal effects. The reproducibility of these effects is usually poor, and no physiologic or pathogenic mechanism, so far, has been found to explain the alleged effects. Equally, epidemiologic studies have not furnished clear and reproducible data as arguments for negative health effects. Final results of the INTERPHONE study on the risk of brain tumours, acoustic neurinoma and parotid gland tumours associated with the use of mobile phones will be soon available. Preliminary results do not seem to indicate a substantial increase in risk. There are presently no scientific data supporting the concept of a special vulnerability of children and adolescents to high-frequency EMF, even if the usual caveats (developing organisms and structures may be more vulnerable, decades of life to come) are considered. The concept of precautionary measures adapted to such concerns is critically discussed.

(E)Panagopoulos DJ, Karabarbounis A, Lioliousis C. ELF alternating magnetic field decreases reproduction by DNA damage induction. Cell Biochem Biophys 67(2):703-716, 2013. (CE, GE, ME, PN, VO)

In the present experiments, the effect of 50-Hz alternating magnetic field on Drosophila melanogaster reproduction was studied. Newly eclosed insects were separated into identical groups of ten males and ten females and exposed to three different intensities of the ELF magnetic field (1, 11, and 21 G) continuously during the first 5 days of their adult lives. The

reproductive capacity was assessed by the number of F1 pupae according to a well-defined protocol of ours. The magnetic field was found to decrease reproduction by up to 4.3%. The effect increased with increasing field intensities. The decline in reproductive capacity was found to be due to severe DNA damage (DNA fragmentation) and consequent cell death induction in the reproductive cells as determined by the TUNEL assay applied during early and midoogenesis (from germarium to stage 10) where physiological apoptosis does not occur. The increase in DNA damage was more significant than the corresponding decrease in reproductive capacity (up to ~7.5%). The TUNEL-positive signal denoting DNA fragmentation was observed exclusively at the two most sensitive developmental stages of oogenesis: the early and midoogenesis checkpoints (i.e. region 2a/2b of the germarium and stages 7-8 just before the onset of vitellogenesis)-in contrast to exposure to microwave radiation of earlier work of ours in which the DNA fragmentation was induced at all developmental stages of early and mid-oogenesis. Moreover, the TUNEL-positive signal was observed in all three types of egg chamber cells, mainly in the nurse and follicle cells and also in the oocyte, in agreement with the microwave exposure of our earlier works. According to previous reports, cell death induction in the oocyte was observed only in the case of microwave exposure and not after exposure to other stress factors as toxic chemicals or food deprivation. Now it is also observed for the first time after ELF magnetic field exposure. Finally, in contrast to microwave exposure of previous experiments of ours in which the germarium checkpoint was found to be more sensitive than stage 7-8, in the magnetic field exposure of the present experiments the mid-oogenesis checkpoint was found to be more sensitive than the germarium.

(E)Qi G, Zuo X, Zhou L, Aoki E, Okamula A, Watanebe M, Wang H, Wu Q, Lu H, Tuncel H, Watanab H, Zeng S, Shimamoto F. Effects of extremely low-frequency electromagnetic fields (ELF-EMF) exposure on B6C3F1 mice. Environ Health Prev Med 20(4):287-293, 2015.(CE, IU, M, ME, PN, VO)

Objective: Long-term exposure study was conducted to investigate the effects of extremely lowfrequency electromagnetic field on the tumor promotion process and fertility. **Methods:** Ten pregnant C57BL/6NCrj mice were exposed to 50 Hz field 500 mG for 1 week (12 h per day), and 24 male and 42 female B6C3F1mice born from them were further exposed up to 15.5 months. As a control group, 10 pregnant mice were bred without exposure, and 30 produced male and 32 female mice were observed without exposure for the same period. **Results:** Mean body weights of exposed groups of male and female mice were decreased significantly than those of the control groups. In exposed mice, there was no increased incidence of liver and lung tumor. In female mice, the incidence of chronic myeloid leukemia [3/42 (7%)] in the exposed group was significantly greater than in the control group. <u>The size of seminiferous tubules in the</u> <u>EMF exposed groups were significantly less than the control group</u>. **Conclusions:** These data support the hypothesis that long-term exposure of 50 Hz magnetic fields is a significant risk factor for neoplastic development and fertility in mice.

(E)Ramadan LA, Abd-Allah AR, Aly HA, Saad-el-Din AA. Testicular toxicity effects of magnetic field exposure and prophylactic role of coenzyme Q10 and L-carnitine in mice. Pharmacol Res. 46(4):363-370, 2002. (CE, FC, IX, M, ME, VO)

The protective effect of L-carnitine or coenzyme Q10 (CoQ10) against high magnetic field (20 mT) induced testicular toxicity in mice were evaluated. Animals were injected with L-carnitine (200 mg kg(-1), i.p.) or CoQ10 (200 mg kg(-1), p.o.) 1h before exposure to fractionated doses (30 min per day, three times per week for 2 weeks) or acute dose (3h) of magnetic field. Total sperm count, motility, daily sperm production, and testicular LDH-X activity as well as histopathological examination were investigated. Exposure of mice to fractionated doses of magnetic field caused a significant decrease in sperm count, motility, daily sperm production, and LDH-X activity, which was more pronounced than that of acute dose. Moreover, a marked testicular histopathological changes were observed after exposure to fractionated doses of magnetic field. Pretreatment of mice with L-carnitine or CoQ10 1h before exposure to magnetic field (20 mT).

(E)Rasaeifar K, Zavareh S, Hajighasem-Kashani M, Nasiri M. Effects of pulsed electromagnetic fields and N-acetylcysteine on transplantation of vitrified mouse ovarian tissue. Electromagn Biol Med 42(2):67-80, 2023. (CE, F, GE, IX, ME, VO)

In this experimental study, adult female NMRI mice were randomly assigned to five groups: control; (fresh ovarian transplantation, OT); sham ;(vitrified OT); NAC ;(vitrified OT treated with N-acetyl cysteine, NAC); EMF ;(vitrified OT treated with pulsed electromagnetic fields, PEMF); and NAC+EMF ;(vitrified OT combined with NAC and PEMF). We conducted histological assessments to evaluate follicle reservation and vascularization. Furthermore, we examined the relative expression of Fgf-2, Vegf, Tnf-a, Il-6, Il-1, and Cd31 genes on days 2 and 7 after OT. Additionally, we measured total antioxidant capacity (TAC), malondialdehyde (MDA) levels, as well as the activity of superoxide dismutase (SOD) and glutathione peroxidase (GPX). Our results demonstrated that NAC, PEMF, and NAC+PEMF treatments significantly increased the number of follicles. Moreover, we observed a more pronounced development of vascularization in the NAC, PEMF, and PEMF+NAC groups. The relative expression levels of Fgf-2, Vegf, Tnf-a, Il-1B, and Il-6 were significantly elevated in the NAC, PEMF, and NAC+PEMF groups. Notably, TAC levels decreased significantly in the NAC group compared to the control group. Additionally, the MDA level showed a significant decrease in the PEMF+NAC group when compared to the other groups. Overall, the combination of NAC and PEMF exhibited a synergistic effect in promoting angiogenesis and protecting against oxidative stress and inflammation during OT.

(E)Ren Y, Chen J, Miao M, Li D-K, Liang H, Wang Z, Yang F, Sun X, Yuan W. Prenatal exposure to extremely low frequency magnetic field and its impact on fetal growth. Environ Health 18(1):6, 2019. (CE, DE, HU, IU)

Objective: Studies on the effect of prenatal exposure to magnetic field (MF) on fetal growth is inconclusive and subject to some methodological limitations, particularly in measurement of MF exposure. The present study aimed to examine the association between maternal extremely low frequency MF (ELF-MF) exposure during pregnancy and fetal growth in offspring. **Methods:** A total of 128 pregnant women were recruited at their 3rd trimester and asked to wear an EMDEX Lite meter for 24 h to capture daily ELF-MF exposure. Time-weighted average (TWA), P50, and

P75 of personal 24-h measurements were used to evaluate prenatal ELF-MF exposure. The medians of these measurements were used as cut-off points of high and low prenatal ELF-MF exposure. Fetal growth was measured by infant's birth weight, skinfold thickness of triceps, abdomen, and back, and circumference of head, upper arm, and abdomen. These measures were conducted within 24-h after birth. Generalized Linear Model was used to examine the association between maternal ELF-MF level and fetal growth indices after potential confounders were adjusted for. **Results:** Compared with girls with lower prenatal ELF-MF exposure, girls with higher exposure had a lower birth weight, thinner skinfold of triceps, abdomen and back, and smaller circumference of head, upper arm and abdomen in all three ELF-MF matrices. The differences were statistically significant for birth weight and most other growth measurements (P < 0.05). These measures had no significant difference between higher and lower prenatal ELF-MF exposure to higher ELF-MF levels was associated with decreased fetal growth in girls, but not in boys

(E)Roychoudhury S, Jedlicka J, Parkanyi V, Rafay J, Ondruska L, Massanyi P, Bulla J. Influence of a 50 hz extra low frequency electromagnetic field on spermatozoa motility and fertilization rates in rabbits. J Environ Sci Health A Tox Hazard Subst Environ Eng. 44(10):1041-1047, 2009.(AE, DE, FC, IV, M, VO) (exposure time= 20 min)

Effects of a 50 Hz extra-low frequency electromagnetic field (ELF EMF) on in vitro rabbit spermatozoa motility were analyzed, as well as the effect on fertilization rates after insemination. Pooled semen samples and a control were exposed to 50 Hz ELF EMF. The difference of the samples of the test groups G1 and G2 with the control group CG (75.56%) for spermatozoa motility were found to be significant (P < 0.01). Differences were significant (P < 0.01) for curvilinear velocity (VCL) between the test group G3 (122.38 microm/s) and the control group CG (112.02 microm/s). Hormonally stimulated adult (9-12 months) females (n = 140) were inseminated with semen samples from G1, G2, G3 and CG (0.88 x 109 spermatozoa/0.5 mL average insemination portion) immediately after ELF EMF exposure and fertilization (kindling) rates were calculated. For the G2 it was 54.28% data indicate <u>50 Hz ELF EMF induced</u> alterations of spermatozoa motility and kindling rate in rabbits, therefore influencing fertility.

(NE)Ruan G, Liu X, Zhang Y, Wan B, Zhang J, Lai J, He M, Chen C. Power-frequency magnetic fields at 50 Hz do not affect fertility and development in rats and mice. Electromagn Biol Med 38(1):111-122. 2019.(CE, DE, F, FC, M, VO)

In the present study, the effects of power-frequency magnetic fields (PF-MF) on fertility and development were investigated in rats and mice. Adult Sprague-Dawley rats and C57BL/6J mice were divided into four groups: a sham exposure group and $30-\mu$ T, $100-\mu$ T and $500-\mu$ T PF-MF exposure groups. The rats were exposed for 24 weeks, and the exposure time for mice ranged from 18 d to 12 weeks, dependent on the different investigated end points. The rats and mice were exposed for 20 h/d. Plasma hormone levels in rats and mice were analyzed. Furthermore, pregnancy rates and implanted embryos were recorded in pregnant mice. Finally, the neonatal growth of mice was evaluated. The results showed that none of the three intensities affected the body weight and paired ovary weight in female rats. Meanwhile, none of the three intensities affected the body weight, weights of paired testes, weights of paired epididymis and sperm count in male rats. Similarly, no significant differences were found in plasma sex hormone levels

between the different PF-MF exposure groups and the sham exposure group. In addition, the pregnancy rates and implanted embryos were not significantly different between the four groups. Moreover, PF-MF exposures had no effects on either the number of fetuses in pregnant mice or the growth and development of neonatal mice.

Santini SJ, Cordone V, Falone S, Mijit M, Tatone C, Amicarelli F, Di Emidio G. Role of Mitochondria in the Oxidative Stress Induced by Electromagnetic Fields: Focus on Reproductive Systems. Oxid Med Cell Longev 2018:5076271, 2018. (Review)

Erratum in

 Corrigendum to "Role of Mitochondria in the Oxidative Stress Induced by Electromagnetic Fields: Focus on Reproductive Systems".
Santini SJ, Cordone V, Falone S, Mijit M, Tatone C, Amicarelli F, Di Emidio G.Oxid Med Cell Longev. 2020 May 17;2020:5203105. doi: 10.1155/2020/5203105. eCollection 2020.PMID: 32566087

Modern technologies relying on wireless communication systems have brought increasing levels of electromagnetic field (EMF) exposure. This increased research interest in the effects of these radiations on human health. There is compelling evidence that EMFs affect cell physiology by altering redox-related processes. Considering the importance of redox milieu in the biological competence of oocyte and sperm, we reviewed the existing literature regarding the effects of EMFs on reproductive systems. Given the role of mitochondria as the main source of reactive oxygen species (ROS), we focused on the hypothesis of a mitochondrial basis of EMF-induced reproductive toxicity. MEDLINE, Web of Science, and Scopus database were examined for peer-reviewed original articles by searching for the following keywords: "extremely low frequency electromagnetic fields (ELF-EMFs)," "radiofrequency (RF)," "microwaves," "Wi-Fi," "mobile phone," "oxidative stress," "mitochondria," "fertility," "sperm," "testis," "oocyte," "ovarian follicle," and "embryo." These keywords were combined with other search phrases relevant to the topic. Although we reported contradictory data due to lack of uniformity in the experimental designs, a growing body of evidence suggests that EMF exposure during spermatogenesis induces increased ROS production associated with decreased ROS scavenging activity. Numerous studies revealed the detrimental effects of EMFs from mobile phones, laptops, and other electric devices on sperm quality and provide evidence for extensive electron leakage from the mitochondrial electron transport chain as the main cause of EMF damage. In female reproductive systems, the contribution of oxidative stress to EMF-induced damages and the evidence of mitochondrial origin of ROS overproduction are reported, as well. In conclusion, mitochondria seem to play an important role as source of ROS in both male and female reproductive systems under EMF exposure. Future and more standardized studies are required for a better understanding of molecular mechanisms underlying EMF potential challenge to our reproductive system in order to improve preventive strategies.

(E)Strand JA, Abernethy CS, Skalski JR, Genoway RG. Effects of magnetic field exposure on fertilization success in rainbow trout, Salmo gairdneri. Bioelectromagnetics. 1983;4(4):295-301, 1983. (AE, F, FC, IV, M)

The sensitivity of trout ova and sperm to 1-T magnetic fields was investigated. It was determined that 1) overall test results combining seven independent Z-statistics demonstrated a significant (alpha less than 0.0001) enhancement of fertilization when ova alone were exposed to the magnetic field prior to fertilization; 2) similarly, overall test results combining Z-statistics from eight independent experiments indicated a significant (alpha less than 0.0004) enhancement when sperm alone were exposed; and 3) statistical analysis of nine independent experiments confirmed enhanced fertilization (alpha less than 0.0001) when both ova and sperm were exposed to the magnetic field prior to fertilization. <u>Although these data indicated that both ova and sperm were sensitive to magnetic fields, simultaneous exposure of both gametes did not have a greater total effect on fertilization rate than the sum of their individual effects.</u>

(E) Su L, Zhao C, Jin Y, Lei Y, Lu L, Chen G. Association between parental occupational exposure to extremely low frequency magnetic fields and childhood nervous system tumors risk: A meta-analysis. Sci Total Environ 642:1406-1414, 2018. (CE, HU) (parental exposure, analysis of previous data)

Background and objective: Previous epidemiological studies suggested association between parental occupational exposure to extremely low frequency magnetic fields (ELF-MF) and risk of childhood nervous system tumors, but the results were inconsistent. We conducted a metaanalysis of case-control and cohort studies to re-evaluate this association. Methods: Relevant studies were identified by searching PubMed and Web of Science databases as well as by manual searching. Summary odds ratio (OR) with 95% confidence interval (CI) were pooled with a fixed-effects or random-effects model. Results: A total of 22 eligible articles (21 case-control studies and 1 cohort study) were included for the quantitative analysis. The results showed that parental occupational ELF-MF exposure was significantly associated with an increased risk of childhood nervous system tumors (OR = 1.11, 95% CI = 1.02-1.21), and this association remained in studies on central nervous system (CNS) tumors (OR = 1.13, 95% CI = 1.02-1.27) but not neuroblastoma (OR = 1.02, 95% CI = 0.92-1.14). Furthermore, maternal (OR = 1.14, 95% CI = 1.05-1.23) but not paternal (OR = 1.05, 95% CI = 0.98-1.13) occupational ELF-MF exposure significantly increased risk of childhood nervous system tumors. Increased risk of childhood CNS tumors was significant associated with maternal (OR = 1.16, 95% CI = 1.06-1.26) but not paternal (OR = 1.15, 95% CI = 0.98-1.34) occupational ELF-MF exposure. Conclusion: In conclusion, our results provide limited evidence for the association between maternal occupational exposure to ELF-MF and increased risk of childhood CNS tumors, which should be explained with cautions. Future studies are needed to further evaluate the association of paternal occupational ELF-MF exposure with risk of childhood CNS tumors.

(NE)Su L, Zhu L, Liu Z, Lou J, Han B, Lin C, Li D, Qian J, Zhao X, Chen G.The decreased permittivity of zebrafish embryos culture medium by magnetic fields did not affect early development of zebrafish embryos. Ecotoxicol Environ Saf 193:110350, 2020. (CE, DE, IU)

Epidemiological studies have shown associations between exposure to environmental extremely low frequency magnetic fields (ELF-MF) and health effects, but the mechanisms of ELF-MF induced biological effects remain unclear. We hypothesized that ELF-MF may regulate functions of tissues or cells via its effects on surrounding environment, e.g., culture medium. To test this hypothesis, we investigated the effects of 50 Hz MF on the relative permittivity of zebrafish embryos culture medium as well as of MF-exposed medium on zebrafish embryos development. The responses of medium to 50 Hz MF exposure were evaluated by a phase-sensitive surface plasmon resonance (SPR) system. The results demonstrated that MF treatment decreased relative permittivity of zebrafish embryos medium in a dose and time-dependent way. Interestingly, the decreased permittivity induced by MF exposure gradually recovered and approached to the base level when the exposure was removed off. However, <u>MF-exposed medium did not trigger</u> adverse consequences of embryos during zebrafish embryonic development, including mortality, malformation, hatching and heart rate when the MF pre-exposed medium was subjected to one cell-stage embryos. Moreover, the MF-exposed medium did not induce apoptosis of zebrafish embryos at 48 and 72 h post fertilization. Our data demonstrated that the relative permittivity of zebrafish embryos medium was decreased by MF exposure, whereas this decrease failed to result in abnormal development of zebrafish embryos.

(NE)Sun YL, Zhou WJ, Wu JQ, Gao ES. Does exposure to computers affect the routine parameters of semen quality? Asian J Androl. 7(3):263-266, 2005. (CE, FC, HU, M, ME)

AIM: To assess whether exposure to computers harms the semen quality of healthy young men. METHODS: A total of 178 subjects were recruited from two maternity and children healthcare centers in Shanghai, 91 with a history of exposure to computers (i.e., exposure for 20 h or more per week in the last 2 years) and 87 persons to act as control (no or little exposure to computers). Data on the history of exposure to computers and other characteristics were obtained by means of a structured questionnaire interview. Semen samples were collected by masturbation in the place where the semen samples were analyzed. RESULTS: No differences in the distribution of the semen parameters (semen volume, sperm density, percentage of progressive sperm, sperm viability and percentage of normal form sperm) were found between the exposed group and the control group. Exposure to computers was not found to be a risk factor for inferior semen quality after adjusting for potential confounders, including abstinence days, testicle size, occupation, history of exposure to toxic substances. CONCLUSION: The present study did not find that healthy men exposed to computers had inferior semen quality.

(E)Suri S, Dehghan SF, Sahlabadi AS, Ardakani SK, Moradi N, Rahmati M, Tehrani FR. Relationship between exposure to Extremely Low-Frequency (ELF) magnetic field and the level of some reproductive hormones among power plant workers. J Occup Health 62(1):e12173, 2020. (CE, HU, MO)

Background and aims: Today, human beings are exposed to the ELF magnetic field of electrical equipment and power lines, which can damage Leydig cells and alter the secretion of reproductive hormones. The purpose of this study was to investigate the relationship between exposure to ELF magnetic field and the level of some reproductive hormones in male power plant workers. **Materials and methods:** The present cross-sectional study was carried out among all male employees of different units of the selected power plant around Tehran, Iran. All participants were asked to complete demographic data sheets and General Health questionnaire, on condition of consent and meeting the inclusion criteria. Time-weighted average (TWA) exposure to magnetic field of 122 men was measured by IEEE Std C95.3.1 method using TES

1393 Gauss meter. Based on the exposure level, subjects were divided into three groups. Serum Levels of Free Testosterone, Luteinizing Hormone (LH), and Follicle stimulating hormone (FSH) in participants were determined. Data analysis was performed using ANOVA, Kruskal-Wallis tests, and the relationships between variables were assessed by linear regression and correlation using SPSS v.25 software. **Results:** There was no significant statistical correlation between the level of ELF exposure and serum levels of free testosterone, LH, and FSH, (r = 0.158). Serum levels of LH decreased significantly with age and duration of work experience (P < .05, r = -.25, P = .005, r = -.203, P = .025). **Conclusion:** There was no relationship between exposure to magnetic field in power plants and reproductive hormone levels, although it is impossible to make definitive comments without using more accurate methods to estimate male fertility.

(E)Tablado L, Pérez-Sánchez F, Soler C. Is sperm motility maturation affected by static magnetic fields? Environ Health Perspect. 104(11):1212-1216, 1996. (CE, FC, M, VO)

Kinematic parameters were evaluated in mouse epididymal extracts to monitor maturation of sperm movement in animals exposed to static magnetic fields using the Sperm-Class Analyzer computerized image analysis system. For this purpose, animals were exposed to a field of 0.7 T generated by a permanent magnet over 10 or 35 days for either 1 or 24 hr/day. The values of the motion endpoints were similar in animals used as controls and in those exposed to the nonionizing radiation, whatever the period of exposure or daily dosage. <u>Changes in motility were observed in all groups: the percentage of total motile and progressive motile spermatozoa increased during passage through the epididymis, with major changes between the caput and corpus epididymides, and the pattern of swimming changed clearly towards more rapid and straighter trajectories. The processes of initiation of sperm motility and maturation of displacement patterns were not then affected by magnetic treatment. Moreover, it appears that sperm production is unaffected because no changes were observed in testicular or epididymal weights after exposure to static magnetic fields.</u>

(E) Tablado L, Pérez-Sánchez F, Núñez J, Núñez M, Soler C. Effects of exposure to static magnetic fields on the morphology and morphometry of mouse epididymal sperm. Bioelectromagnetics. 19(6):377-383, 1998. (CE, M, ME, VO)

Morphologic and morphometric sperm characteristics of mouse epididymal extracts from animals exposed to static magnetic fields were evaluated. For this purpose, animals were exposed for 35 days to a field of 0.7 T generated by a commercial permanent magnet for either 1 or 24 h per day. The values of morphometric parameters were obtained using the morphometric module of the Sperm Class Analyzer computerized image analysis system, and percentages of abnormalities were calculated. The size of sperm heads was unaffected by exposure to static magnetic fields. Lack of hook was a sperm head abnormality found significantly more frequently in animals exposed continually than in nonexposed animals, showing a possible alteration to the spermatogenic process after exposure to static magnetic fields. The percentage of sperm with coiled tails or of sperm with abnormal midpiece or tail was not altered by exposure.

(NE)

Talibov M, Olsson A, Bailey H, Erdmann F, Metayer C, Magnani C, Petridou E, Auvinen

A, Spector L, Clavel J, Roman E, Dockerty J, Nikkilä A, Lohi O, Kang A, Psaltopoulou T, Miligi L, Vila J, Cardis E, Schüz J. Parental occupational exposure to low-frequency magnetic fields and risk of leukaemia in the offspring: findings from the Childhood Leukaemia International Consortium (CLIC). Occup Environ Med 76(10):746-753, 2019. (CE, HU) (Parental exposure and cancer)

Objectives: Previously published studies on parental occupational exposure to extremely lowfrequency magnetic fields (ELF-MF) and risk of acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML) in their offspring were inconsistent. We therefore evaluated this question within the Childhood Leukemia International Consortium. **Methods:** We pooled 11 case-control studies including 9723 childhood leukaemia cases and 17 099 controls. Parental occupational ELF-MF exposure was estimated by linking jobs to an ELF-MF job-exposure matrix (JEM). Logistic regression models were used to estimate ORs and 95% CIs in pooled analyses and meta-analyses. **Results:** ORs from pooled analyses for paternal ELF-MF exposure >0.2 microtesla (μ T) at conception were 1.04 (95% CI 0.95 to 1.13) for ALL and 1.06 (95% CI 0.87 to 1.29) for AML, compared with ≤0.2 μ T. Corresponding ORs for maternal ELF-MF exposure during pregnancy were 1.00 (95% CI 0.89 to 1.12) for ALL and 0.85 (95% CI 0.61 to 1.16) for AML. No trends of increasing ORs with increasing exposure level were evident. Furthermore, no associations were observed in the meta-analyses. **Conclusions:** In this large international dataset applying a comprehensive quantitative JEM, we did not find any associations between parental occupational ELF-MF exposure and childhood leukaemia.

(NE)Tateno H, Iijima S, Nakanishi Y, Kamiguchi Y, Asaka A. No induction of chromosome aberrations in human spermatozoa exposed to extremely low frequency electromagnetic fields. Mutat Res. 414(1-3):31-35, 1998. (AE, GE, IV, M)

Clastogenic effects of extremely low frequency electromagnetic fields (ELF-EMFs) on human sperm chromosomes were studied using an interspecific in vitro fertilization system with zonafree golden hamster oocytes. Semen samples from healthy men were exposed to ELF-EMFs (50 Hz, 20 mT) for 2 h at 37 degreesC under 5% CO₂ in air. The samples were then cryopreserved in liquid nitrogen for shipment to a cytogenetic laboratory. After thawing the samples, motile spermatozoa were collected using a continuous Percoll density gradient centrifugation and then capacitated for in vitro fertilization with hamster oocytes. Sperm-derived chromosomes were analyzed at first cleavage metaphase. The present experiment was performed twice using semen samples from two different donors. In test-1, incidence of spermatozoa that displayed structural chromosome aberrations was 17.0% (35/206) in the exposed group and 20.8% (55/264) in the control group. In test-2, structural chromosome aberrations were observed in 11.1% (13/117) of exposed spermatozoa and 13.8% (13/94) of spermatozoa in the control group. In both tests, there was no significant difference in the incidence of chromosomally abnormal spermatozoa between the exposed group and the control group. Types of aberrations observed and their incidences per spermatozoon in the exposed group were similar to those of the control group. Despite the small sample size, the present results suggest that ELF-EMFs have no clastogenic effect on human sperm chromosomes.

(NE)Törnqvist S. Paternal work in the power industry: effects on children at delivery. J Occup Environ Med. 40(2):111-117, 1998. (CE, DE, HU) (parental exposure) Although reports on reproductive disturbances among occupational groups of electrical workers have been discussed, few studies have focused explicitly on the children of workers employed in the power industry. Birth outcome and cancer in the offspring of fathers who were exposed to electric and magnetic fields at time of sperm production were studied in two cohorts. In Study 1, male occupation in the power industry was identified in censuses. Study 2 is a prospective cohort study of newly employed power industry workers. Birth data were obtained by record linkage between censuses and several available health registers in Sweden. Multiple births, birth weight, sex, survival, congenital malformations, and cancer have been analyzed with relation to the father's exposure to electric and magnetic fields one year before the child was born. There were six cancer cases among infants in the exposed group (2.4 expected) and six in the unexposed group (3.2 expected) in Study 1. Jointly, the 12 cancer cases found among the infants were more than expected (P = 0.02). However, this total excess may be random. No cancer cases were observed in the prospective study. For chromosomal abnormalities, such as Down's syndrome, one case was observed among infants of exposed fathers and three cases among unexposed fathers in Study 1. In Study 2, no cases were observed. There was a slightly higher proportion of malformation diagnoses among infants of exposed fathers than among infants of unexposed fathers in Study 2, but this could be random (odds ratio = 1.59; 95% Confidence interval 0.43-1.48). No clear-cut effects on infants fathered by men who were exposed to electric and magnetic fields around the time of sperm production could be seen in these two studies.

(E) Torres L, Guevara B, Cruz V, Valdivia M. Myrciaria dubia "camu camu" flour as a magnetoprotector in male mouse infertility. Bioelectromagnetics 40(2):91-103, 2019. (CE, FC, M, ME, VO) (50 Hz, 24 h/day, 5 weeks)

Possible adverse effects of extremely low frequency magnetic fields (ELF-MF) are linked to a decrease of antioxidant defenses and the production of free radicals. The increase of free radicals affects the mitochondrial functionality inducing apoptosis, which affects the phosphorylation and generation of key ATP in fertilization. Myrciaria dubia, known as "camu camu," is a fruit with high levels of ascorbic acid, which exerts an important antioxidant function in the prevention of premature cell damage. In this study, the effect of Myrciaria dubia flour on oxidative damage produced by ELF-MF (610 μ T) was evaluated by detecting the activity of endogenous mitochondrial oxidoreductase enzymes in a complete sperm cycle of mice. We found that the MF caused a significant (P < 0.05) decrease in sperm quality, whereas the groups supplied with Myrciaria dubia flour (50 and 75 mg/kg of body mass) in ELF-MF exposure showed a significant recovery (P < 0.05) in parameters of viability, percentage of plasma membrane integrity and mitochondrial activity, and index of epidymal sperm. This suggests that Myrciaria dubia flour would have an antioxidant activity that counteracts the damaging effects of ELF-MF in spermatogenesis and could be used as a natural ELF-MF protector.

(NE)Veicsteinas A, Belleri M, Cinquetti A, Parolini S, Barbato G, Molinari Tosatti MP Development of chicken embryos exposed to an intermittent horizontal sinusoidal 50 Hz magnetic field. Bioelectromagnetics17(5):411-424, 1996. (CE, DE, IU)

The effects of intermittent exposure (2 h on/22 h off) to a 200 microT horizontal, sinusoidally oscillating (50 Hz) magnetic field were studied in 210 fertilized chicken eggs. Two hundred ten control eggs (sham-exposed) were incubated in the same chamber as the experimental eggs.

Chick embryos were examined for developmental anomalies and maturity stage after 48 h of incubation. Immunohistochemical analysis of extracellular membrane components (laminin, fibronectin, and type IV collagen) were conducted on day 7 and histological examinations for malformations of brain, liver, and heart, on days 7, 12, and 18 of incubation. Furthermore, egg fertility and egg weights were evaluated on days 2, 7, 12, and 18. The investigation also measured the body weight of chickens for 90 days from hatching and included histological analysis of body organs. Each variable was investigated blind. Statistical comparison between exposed and sham-exposed values did not show significant differences in any of the variables investigated. Thus, it appears that the exposure of embryos to an intermittent 200 microT magnetic field at 50 Hz does not cause developmental anomalies, changes in maturity stage, alterations in distribution of extracellular membrane components, or malformations in the brain, liver, or heart. Moreover, there were no differences in body weight, morphology, or histology of central nervous system, liver, heart, or testis in 90-day-old chickens hatched from exposed in comparison to sham-exposed eggs.

(E)Wang XW, Ding GR, Shi CH, Zeng LH, Liu JY, Li J, Zhao T, Chen YB, Guo GZ. Mechanisms involved in the blood-testis barrier increased permeability induced by EMP. Toxicology. 276(1):58-63, 2010. (AE, FC, M, ME, MO, VO)

The blood-testis barrier (BTB) plays an important role in male reproductive system. Lots of environmental stimulations can increase the permeability of BTB and then result in antisperm antibody (AsAb) generation, which is a key step in male immune infertility. Here we reported the results of male mice exposed to electromagnetic pulse (EMP) by measuring the expression of tight-junction-associated proteins (ZO-1 and Occludin), vimentin microfilaments, and transforming growth factor-beta (TGF-beta3) as well as AsAb level in serum. Male BALB/c mice were sham exposed or exposed to EMP at two different intensities (200kV/m and 400kV/m) for 200 pulses. The testes were collected at different time points after EMP exposure. Immunofluorescence histocytochemistry, western blotting, laser confocal microscopy and RT-PCR were used in this study. Compared with sham group, the expression of ZO-1 and TGF-beta3 significantly decreased accompanied with unevenly stained vimentin microfilaments and increased serum AsAb levels in EMP-exposed mice. <u>These results suggest a potential BTB injury and immune infertility in male mice exposed to a certain intensity of EMP.</u>

(E)Wydorski PJ, Kozlowska W, Drzewiecka, EM, Zmijewska A, Franczak A. Extremely low-frequency electromagnetic field exposure alters DNA methylation levels in the endometrium of pigs during the peri-implantation period. Reprod Fertil Dev 35(12):601-613, 2023. (AE, F, GE, IV)

Context: Extremely low-frequency electromagnetic field (ELF-EMF) emission is increasing due to substantial technological progress. The results of previous research provided evidence that ELF-EMF may exert changes in molecular mechanisms that control female reproduction. **Aims:** We hypothesised that short-term ELF-EMF treatment alters the DNA methylation level of genes in the endometrium. Hence, the research aimed to determine the methylation level of selected genes whose expression was altered in response to ELF-EMF radiation in the endometrium of pigs during the peri-implantation period (days 15-16 of pregnancy). **Methods:** Porcine endometrial slices (100±5mg) were collected during the peri-implantation

period and exposed to ELF-EMF at a frequency of 50Hz for 2h in vitro. The control endometrium was not exposed to ELF-EMF. The level of DNA methylation in the promoter regions of EGR2, HSD17B2, ID2, IL1RAP, MRAP2, NOS3, PTGER4, SERPINE1, VDR and ZFP57 was tested using qMS-PCR. **Key results:** In the endometrium exposed to ELF-EMF, the level of methylation of HSD17B2, MRAP2, SERPINE1, VDR and ZFP57 was not altered; the level of methylation of EGR2, ID2 and PTGER4 increased, and the level of methylation of IL1RAP and NOS3 decreased. **Conclusions:** ELF-EMF may alter the level of DNA methylation in the endometrium during the peri-implantation period. **Implications:** Changes in the DNA methylation induced by ELF-EMF may affect the transcriptomic profile of the endometrium and disturb physiological processes accompanying implantation and embryo development.

(E) Wydorski PJ, Kozlowska W, Zmijewska A, Franczak A. Exposure to the extremely low-frequency electromagnetic field induces changes in the epigenetic regulation of gene expression in the endometrium. Theriogenology 217:72-82, 2024. (AE, F, GE, IV) (8 mT, 2 h)

Increasing technological development results in more sources of the extremely low-frequency electromagnetic field (ELF-EMF), which is recognized as an environmental risk factor. The results of the past study indicate that the ELF-EMF can affect the level of DNA methylation. The study aimed to determine whether the ELF-EMF induces changes in epigenetic regulation of gene expression in the endometrium of pigs during the peri-implantation period. Endometrial slices (100 \pm 5 mg) collected on days 15-16 of pregnancy were exposed in vitro to the ELF-EMF at a frequency of 50 Hz for 2 h of treatment duration. To determine the impact of the ELF-EMF on elements of epigenetic regulations involved in DNA methylation, histone modification, and microRNA biogenesis in the endometrium, the DNMT1 and DNMT3a; EZH2, UHRF1, and MBD1; DICER1 and DGCR8 mRNA transcript and protein abundance were analyzed using Real-Time PCR and Western blot, respectively. Moreover, EED and SUZ12 mRNA transcript, global DNA methylation, and the activity of histone deacetylase (HDAC) were analyzed. The changes in the abundance of DNMT1 and DNMT3a, EZH2 mRNA transcript and protein, EED and SUZ12 mRNA transcript, global DNA methylation level, HDAC activity, and the abundance of proteins involved in microRNA biogenesis evoked by the ELF-EMF in the endometrium were observed. The ELF-EMF possesses the potential to alter epigenetic regulation of gene expression in the porcine endometrium. Observed alterations may be the reason for changes in the transcriptomic profile of the endometrium exposed to the ELF-EMF which in turn may disrupt biological processes in the uterus during peri-implantation.

(E)Yellon SM. 60-Hz magnetic field exposure effects on the melatonin rhythm and photoperiod control of reproduction. Am J Physiol 270(5 Pt 1):E816-821, 1996. (AE, FC, MO, VO)

Adult Djungarian hamsters in long (16 h of light) or short (10 h of light) days for 6 wk were acutely exposed to a 1-G 60-Hz magnetic field (MF) for 15 min 2 h before dark. The nighttime rise in melatonin was delayed and duration reduced in MF-exposed hamsters in both photoperiods compared with sham controls. In a second replicate experiment, MF effects on melatonin rhythm duration were repeated in hamsters in short but not long days, and amplitudes at some clock times differed between the same treatment groups in the two studies. To test the

hypothesis that daily MF abbreviates melatonin rhythm duration and induces a long-day reproductive response, adults in shot days were exposed daily to MF. After 3 wk, pineal and serum melatonin rhythms were the same in MF and sham groups; reproduction remained suppressed. Irrespective of acute MF exposure effects on the melatonin rhythm, daily MF treatment does not alter photoperiodic time measurement or the clock mechanism controlling reproduction. Adaption to environmental MF exposures may be part of a normal physiological mechanism that maintains photoperiodic responsiveness in individuals and a seasonal pattern of reproduction.

Zhang C, Li C, Yang L, Hou W, Du M, Wu T, Chen W. Assessment of Twin Fetal Exposure to Environmental Magnetic and Electromagnetic Fields. Bioelectromagnetics 43(3):160-173, 2022. (Dosimetry)

Fetal development is vital in the human lifespan. Therefore, it is essential to characterize exposure by a series of typical environmental magnetic and electromagnetic fields. In particular, there has recently been a sharp increase in the twin birth rate. However, lack of appropriate models has prohibited dosimetric evaluation, restricting characterization of the impact of these environmental factors on twins. The present study developed two whole-body pregnant models of 31 and 32 weeks of gestation with twin fetuses and explored several typical exposure scenarios, including 50-Hz uniform magnetic field exposure, local 125-kHz magnetic field (MF), and 13.56-MHz electromagnetic field exposure, as well as wideband planewave radiofrequency (RF) exposure from 20 to 6000 MHz. Finally, dosimetric results were derived. Compared to the singleton pregnancy with similar weeks of gestation, twin fetuses were overexposed at 50-Hz uniform MF, but they were probably underexposed in the RF scenarios with frequencies for wireless communications. Furthermore, the twin fetuses manifested large dosimetric variability compared to the singleton, which was attributed to the incident direction and fetal position. Based on the analysis, the dosimetric results over the entire gestation period were estimated. The results can be helpful to estimate the risk of twin-fetal exposure to electromagnetic fields and examine the conservativeness of the international guidelines.

Zhou F, Ma C, Li YJ, Zhang M, Liu W. Effect of extremely low-frequency electromagnetic radiation on pregnancy outcome: A meta-analysis. Afr J Reprod Health 27(5):95-104, 2023. (Review)

Extremely low-frequency electromagnetic radiation (ELF-EMF) are generated by electrical devices and power systems (1 to 300 Hz). Although several studies have demonstrated that ELF-EMF may beassociated with an increased risk of adverse pregnancy outcomes, other studies have shown no evidence of associations. This meta-analysis was conducted to assess the effect of extremely low frequency electromagnetic radiation on pregnancy outcomes. The following electronic bibliographic databases were searched to identify relevant studies: PubMed, Web Of Science, Cochrane library, Embase, EBSCO. In addition, the manual retrieval of relevant references was conducted as a supplement. Select all eligible studies published from Database construction library to March 10, 2021. Search type for queue research on influence of electromagnetic field radiation on pregnancy results. Data were screened and extracted independently by two researchers. Review Manager 5.3 software was used for the meta-analysis.

There was no significant increase in the risk of miscarriage, stillbirth, birth defects and preterm delivery in the pregnant women who lived near the electromagnetic fields compared with the control group. Conclusions: No correlation has been found between maternal ELF-EMF exposure and miscarriage, stillbirth, neonatal birth defects and preterm delivery, while the effects on small gestational age and low birth weight are still uncertain. Related research with high-quality large samples and different regions are still needed for further verification.