

SECTION 13

EVIDENCE FOR BREAST CANCER PROMOTION

(Melatonin Studies in Cells and Animals)

**CL Sage, Sage Associates,
Santa Barbara, CA USA**

**Prepared for the BioInitiative Working Group
July 2007**

TABLE OF CONTENTS

- I. Introduction**
- II. Melatonin and ELF-EMF**
- III. Tamoxifen and ELF-EMF**
- IV. Animal Studies and ELF-EMF**
- V. Epidemiological Studies on Breast Cancer and ELF-EMF**
Female Breast Cancer Studies
- VI. Male Breast Cancer Studies**
- VII. Conclusions**

Introduction

The subject of breast cancer and studies of melatonin has a long and rich history replete with destroyed scientific reputations and career-ending charges of misconduct of scientists who have contributed stellar scientific work that has proved extremely inconvenient for governmental agencies and military and industrial interests (Liburdy). References are given in each section below to facilitate locating the pertinent references for each section.

II. Melatonin and ELF-EMF

Evidence which supports a possible mechanism for ELF-EMF and breast cancer is the consistent finding (in five separate labs) that environmental levels of ELF-EMF can act at the cellular level to enhance breast cancer proliferation by blocking melatonin's natural oncostatic action in MCF-7 cells (Liburdy, 1993; Luben et al, 1996; Morris et al, 1998; Blackman et al, 2001; Ishido, et al, 2001). ELF-EMF levels between 0.6 and 1.2 μ T have been shown to consistently block the protective effects of melatonin.

The series of papers reporting increased breast cancer cell proliferation when ELF-EMF at environmental levels negatively affects the oncostatic actions of melatonin in MCF-7 cells should warrant new public exposure guidelines or planning target limits for the public, and for various susceptible segments of the population.

References

Liburdy, R. P., T. R. Sloma, et al, 1993. ELF magnetic fields, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER+ breast cancer cell proliferation. *J of Pineal Research*. 14: 89-97.

Luben et al, 1996. Replication of 12 mG EMF effects on melatonin responses of MCF-7 breast cancer cells in vitro. Abstract A-1 of the 1996 Annual review of research on biological effects of electric and magnetic fields from the generation, delivery and use of electricity, November 17-21, 1996. San Antonio, Texas, p.1

Luben et al, 1998. Independent replication of 60-Hz 1.2 μ T EMF effects on melatonin and tamoxifen responses of MCF-7 cells in vitro. Abstract A-3.4, Bioelectromagnetics Society Annual Meeting, St. Pete Beach, FL. June 7-11, p 17-18.

Morris et al, 1998. In vitro exposure of MCF-7 human breast cancer cells to 60-Hz magnetic fields. Abstract p-125A, Bioelectromagnetics Society Annual Meeting, St. Pete Beach, FL. June 7-11, p 204-205.

Ishido et al, 2001. Magnetic fields (MF) of 50 Hz at 1.2 μ T as well as 100 μ T cause uncoupling of inhibitory pathways of adenylyl cyclase mediated by melatonin 1a receptor in MF-sensitive MCF-7 cells.

D.E. Blask, S.M. Hill, Effects of melatonin on cancer: studies on MCF-7 human breast cancer cells in culture, J. Neural Transm. Suppl. 21 (1986) 433–449.

Loberg LI et al 1999. Gene expression in human breast epithelial cells exposed to 60 Hz magnetic fields, Carcinogenesis 20 1633–1636.

III. Tamoxifen and ELF-EMF

Girgert et al (2005) reported that *“the anti-estrogenic activity of tamoxifen is reduced in two subclones of MCF-7 cells under the influence of ELF/EMF to different extent. Dose-response curves of the growth-inhibitory effect of tamoxifen are shifted towards higher concentrations leading to a reduced growth inhibition at a given concentration. Our observations confirm results from a previous report describing a reduced inhibitory effect of tamoxifen at 1^{-7} M from 40% to only 17% by exposure to an EMF of 1.2 μ T”* (Harland et al, 1997). Further, Girgert et al conclude that *“From a medical point of view, it is disturbing that maximal induction of cell proliferation by tamoxifen at a field strength of 1.2 μ T is observed at concentration of 10^{-6} M. This is exactly the serum concentration achieved in BC patients under standard oral therapy.”* (De Cupis et al, 1997).

The Girgert et al paper confirms prior findings that environmental level ELF-EMF inhibits the antiproliferative action of tamoxifen in MCF-7 human breast cancer cells. Four other papers reporting this effect include Liburdy et al, 1997; Harland et al, 1997; Harland et al, 1999; and Blackman et al, 2001).

References

Liburdy et al, 1997. Magnetic Fields, Melatonin, Tamoxifen, and Human Breast Cancer Cell Growth. In: Stevens R. G., Wilson B. W., Anderson L.E. (Eds). The Melatonin Hypothesis - Breast Cancer and Use of Electric Power. Battelle Press, Columbus, Richland 1997: 669- 700.

Harland et al, 1997. Environmental magnetic fields inhibit the antiproliferative action of tamoxifen and melatonin in a human breast cancer cell line. Bioelectromagnetics, 18, 555-562.

Harland et al, 1999. Evidence for a slow time-scale of interaction for magnetic fields inhibiting tamoxifen’s antiproliferative action in human breast cancer cells. Cell Biochemistry & Biophysics, 31(3), 295-306.

Blackman et al, 2001. The influence of 1.2 μ T, 60 Hz magnetic fields on melatonin and tamoxifen-induced inhibition of MCF-7 cell growth. Bioelectromagnetics, 22(2), 122-128.

Girgert et al, 2005. Induction of tamoxifen resistance in breast cancer cells by ELF electromagnetic fields. *Biochemical & Biophysics Research Communications*, 336, 1144-1149.

A. De Cupis et al, 1997. Oestrogen/growth factor cross-talk in breast carcinoma: a specific target for novel antioestrogens, *TIPS* 18 245–251.

IV. Animal Studies and ELF-EMF

Anderson, L. E., G. A. Boorman, et al. (1999). Effect of 13 week magnetic field exposures on DBMA-initiated mammary gland carcinomas in female Sprague-Dawley Rats. *Carcinogenesis*. 20: 1615-1620.

Beniashvili, D. S., V. Bilanishvili, et al. (1991). Low-frequency electromagnetic radiation enhances the induction of rat mammary tumors by nitrosomethyl urea. *Cancer Letters*. 61: 75-79.

Ekstrom, T., K. H. Mild, et al. (1998). Mammary tumours in sprague-dawley rats after initiation with dmbs followed by exposure to 50 Hz electromagnetic fields in a promotional scheme. *Cancer Letters*. 123: 107-111.

Loscher, W., M. Mevissen, et al. (1993). Tumor promotion in a breast cancer model by exposure to a weak alternating magnetic field. *Cancer Letters*. 71: 75-81.

Loscher, W., U. Wahnschaffe, et al. (1994). Effects of weak alternating magnetic fields on nocturnal melatonin production and mammary carcinogenesis in rats. *Oncology*. 51: 288-295.

Mevissen, M., A. Stamm, et al. (1993). Effects of magnetic fields on mammary tumor development induced by 7, 12-dimethylbenz(a)anthracene in rats. *Bioelectromagnetics*. 14: 131-143.

Mevissen M et al, 1995. In vivo exposure of rats to a weak alternating magnetic field increases ornithine decarboxylase activity in the mammary gland by a similar extent as the carcinogen DMBA, *Cancer Lett.* 90 (1995) 207–214.

Mevissen, M., A. Lerchl, et al. (1996). Exposure of DMBA-treated female rats in a 50 Hz, 50 microtesla magnetic field: effects on mammary tumor growth. *Carcinogenesis*. 17: 903-910.

Mevissen, M., A. Lerchl, et al. (1996). Study on pineal function and DMBA-induced breast cancer formation in rats during exposure to a 100-mg, 50 Hz magnetic field. *J of Toxicology & Environmental Health*. 48: 169-185.

Mevissen, M., M. Haussler, et al. (1998). Complex effects of long-term 50 Hz

magnetic field exposure in vivo on immune functions in female Sprague-Dawley rats depend on duration of exposure. *Bioelectromagnetics*. 19: 259-270.

Thun-Battersby, S., M. Mevissen, et al. (1999). Exposure of Sprague-Dawley rats to a 50 Hz, 100 uTesla magnetic field for 27 weeks facilitates mammary tumorigenesis in the

V. Epidemiological Studies on Breast Cancer and ELF-EMF

Female Breast Cancer Studies

References

Milham S. (in press) 2006. Electric typewriter exposure and increased female breast cancer mortality in typists. *Medical Hypotheses*. Elsevier Ltd.

Cantor, K. P., M. Dosemeci, et al. (1995). Re: 'Breast cancer mortality among female electrical workers in the United States' (letter). *J of the National Cancer Institute*. 87: 227-228.

Cantor, K. P., P. A. Stewart, et al. (1995). Occupational exposures and female breast cancer mortality in the United States. *J of Occupational & Environmental Medicine*. 37: 336-348.

Demers, P. and e. al. (1991). Occupational Exposure to Electromagnetic fields and breast cancer in men. *Amer J of Epidemiology*. 134: 340-347.

Coogan, P. F., R. W. Clapp, et al. (1996). Occupational exposure to 60Hz Magnetic Fields and risk of breast cancer in women. *Epidemiology*. 7: 459-464.

Erren, T. (2001). "A meta-analysis of epidemiologic studies of electric and magnetic fields and breast cancer in women and men." *Bioelectromagnetics*(Supplement 5, 2001): S105-S119.

Floderus, B., C. Stenlund, et al. (1999). Occupational magnetic field exposure and site-specific cancer incidence: a Swedish cohort study. *Cancer Causes & Control*. 10: 323-332.

Feychting, M., Forssen, U, L. E. Rutqvist, et al. (1998). Magnetic fields and breast cancer in Swedish adults residing near high-voltage power lines. *Epidemiology*.

Forssen, U. M., M. Feychting, et al. (2000). Occupational and Residential magnetic field exposure and breast cancer in females. *Epidemiology*. 11: 24-29.

Loomis, D. P., D. A. Savitz, et al. (1994). Breast cancer mortality among female electrical workers in the United States. *J of the National Cancer Institute*. 86: 921- 925.

Petralia, S. A., W.-H. Chow, et al. (1998). Occupational risk factors for breast cancer among women in Shanghai. *Amer J Industrial Med*. 34: 477-483.

Rosenbaum, P. F., J. E. Vena, et al. (1994). Occupational exposures associated with male breast cancer. *Amer J of Epidemiology*. 139: 30-36.

Stenlund, C. and B. Floderus (1997). Occupational exposure to magnetic fields in relation to male breast cancer and testicular cancer: a Swedish case-control study. *Cancer Causes & Control*. 8: 184-191.

Tynes, T. H., M; Andersen, A; Vistnes, AL; Haldorsen, T (1996). "Incidence of breast cancer in Norwegian female radio and telegraph operators." *Cancer Causes Control* 7: 197-204.

Tynes et al, 1992. Incidence of cancer in Norwegian workers potentially exposed to electromagnetic fields. *American Journal of Epidemiology*, 136, 81-88.

Vena, J. E., J. L. Freudenheim, et al. (1994). Risk of premenopausal breast cancer and use of electric blankets. *Amer J of Epidemiology*. 140: 974-979.

Verkasalo et al, 1996. Magnetic fields of high voltage power lines and risk of cancer in Finnish adults: nationwide cohort study. *British Medical Journal*, 313(7064), 1047–1051.

VI. Male Breast Cancer Studies

References

Demers et al, 1991. Occupational exposure to electromagnetic fields and breast cancer in men. *American Journal of Epidemiology*, 134, 340-347.

Feychting, M., Forssen, U, L. E. Rutqvist, et al. (1998). Magnetic fields and breast cancer in Swedish adults residing near high-voltage power lines. *Epidemiology*.

Floderus et al, 1999. Occupational magnetic field exposure and site-specific cancer incidence: a Swedish cohort study. *Cancer Causes and Control*, 10, 323-332.

Floderus et al, 1994. Incidence of selected cancers in Swedish railway workers, 1961-1979. *Cancer Causes and Control*, 5, 189-194.

Guenel et al, 1993. Incidence of cancer in persons with occupational exposure to electromagnetic fields in Denmark. *British Journal of Industrial Medicine*, 50, 758-764.

Johansen et al, 1998. Risk of Cancer Among Danish Utility Workers – A Nationwide Cohort Study. *American Journal of Epidemiology*, 147, 548-555.

Loomis et al, 1992. Cancer of breast among men in electrical occupations. *Lancet*, 339, 1482-1483.

Matanowski, G. M., P. N. Breysse, et al. (1991). Electromagnetic field exposure and male breast cancer. *Lancet*. 337: 737.

Stendtlund et al, 1997, Occupational exposure to magnetic fields in relation to male breast cancer and testicular cancer: A Swedish case-control study. *Cancer Causes & Control*, 8, 184-191.

Theriault et al, 1994. . Cancer risks associated with occupational exposure to magnetic fields among electric utility workers in Ontario and Quebec, Canada and France. 1970-1989. *American Journal of Epidemiology*, 139, 550-572.

Tynes et al, 1994. Incidence of cancer among workers in Norwegian hydroelectric power companies. *Scand. J. Work Environ. Health*, 20, 339-344.

VII. Conclusions

Conclusion: The constellation of relevant scientific papers providing mutually-reinforcing evidence for an association between power-frequency electromagnetic fields (ELF-EMF) and breast cancer is strongly supported in the scientific literature.

Conclusion: ELF at environmental levels negatively affects the oncostatic effects of both melatonin and tamoxifen on human breast cancer cells. Numerous epidemiological studies over the last two decades have reported increased risk of male and female breast cancer with exposures to residential and occupational levels of ELF. Animal studies have reported increased mammary tumor size and incidence in association with ELF exposure.

Conclusion: ELF limits for public exposure should be revised to reflect increased risk of breast cancer at environmental levels possibly as low as 2 mG or 3 mG; certainly as low as 4 mG.