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Evidence for an Effect of ELF Electromagnetic Fields on Human Pineal Gland Function

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A study was carried out to determine possible effects of 60-Hz electromagnetic-field exposure on pineal gland function in humans. Overnight excretion of urinary 6-hydroxymelatonin sulfate (6-OHMS), a stable urinary metabolite of the pineal hormone melatonin, was used to assess pineal gland function in 42 volunteers who used standard (conventional) or modified continuous polymer wire (CPW) electric blankets for approximately 8 weeks. Volunteers using conventional electric blankets showed no variations in 6-OHMS excretion as either a group or individuals during the study period. Serving as their own controls, 7 of 28 volunteers using the CPW blankets showed statistically significant changes in their mean nighttime 6-OHMS excretion. The CPW blankets switched on and off approximately twice as often when in service and produced magnetic fields that were 50% stronger than those from the conventional electric blankets. On the basis of these findings, we hypothesize that periodic exposure to pulsed DC or extremely low frequency electric or magnetic fields of sufficient intensity and duration can affect pineal gland function in certain individuals.

Key words: melatonin, electric blankets, electric field, magnetic field

INTRODUCTION

During the past two decades, interest has increased in the possibility that exposure to static or extremely low frequency (ELF: 10–100 Hz), including 50- or 60-Hz powerline-frequency electric and magnetic fields, may cause biological effects in human populations [Savitz and Calle, 1987]. Much of our work has been directed toward understanding the association between ELF electric- and

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magnetic-field exposure and alterations in pineal gland circadian rhythms [Wilson et al., 1989].

Melatonin (N-acetyl-5-methoxytryptamine), the principal hormone of the pineal gland, is produced by the action of N-acetyltransferase (NAT) and hydroxyindole-O-methyl transferase (HIOMT) on serotonin [Deguchi and Axelrod, 1972]. Melatonin concentrations normally increase during the hours of darkness in both the pineal gland and circulating blood. Maximum melatonin concentrations occur between approximately 0200 and 0400 h in humans. In all mammals, the internal clock that helps generate this pineal circadian rhythm resides in the suprachiasmatic nuclei. The pineal is richly innervated by fibers of the superior cervical ganglia (SCG) [Moore et al., 1968] as well as by fibers originating in the hypothalamus and optic regions of the brain [Zisapel et al., 1988]. Neuronal input from the eyes acts via the SCG as the principal regulator of the melatonin circadian rhythm in the pineal.

Light of sufficient intensity is effective in suppressing melatonin synthesis in many animals [Wurtman et al., 1963]. Lewy et al. [1982] reported that the light level required for suppression in humans is approximately 2,500 lux. It appears that the pineal gland of certain sensitive individuals, however, may respond to light levels as low as 200 lux [McIntyre et al., 1990]. Ingested alcohol [Wetterberg, 1978], β-adrenergic receptor-blocking drugs such as propranolol [Wetterberg, 1979], and certain kinds of stress [Troiani et al., 1987] have also been reported to reduce melatonin concentrations in the pineal and circulation of rats. Further, altering melatonin circadian rhythms by use of bright light has been effective in the treatment of seasonal affective disorder syndrome (SADS) [Lewy et al., 1987].

In the circulation, melatonin acts to suppress the function of several other endocrine glands, including the gonads. Melatonin also suppresses the growth of certain cancers in both in vitro and in vivo models [Blask, 1990]. Reduction in melatonin secretion has been associated with estrogen receptor-positive breast cancers [Sanchez Barcelo et al., 1988] and prostate adenocarcinoma [Buzzell et al., 1988]. Stevens [1987] proposed that, should there be increased cancer risk from ELF electromagnetic-field exposure, such risk may be a consequence of altered pineal gland function.

Chronic exposure to 60-Hz electric fields can reduce the normal nocturnal rise in both pineal NAT activity and melatonin concentration in laboratory rats [Wilson et al., 1981, 1983]. In 23-day-old rats maintained in a 60-Hz electric field for 20 h/day from conception, there was no difference among the pineal melatonin levels of animals exposed to field strengths of 10, 60, and 130 kV/m. Compared to controls, however, these exposed rats showed an approximate 40% reduction in maximal nighttime pineal melatonin levels and an approximate 1.4-h delay in the occurrence of the nighttime melatonin peak [Reiter et al., 1988]. Rats first exposed at 55 days of age to a 39-kV/m electric field showed no statistically significant difference between daytime and nighttime levels of pineal melatonin [i.e., no circadian rhythm in melatonin secretion) after 21 days of exposure. Within 3 days after cessation of ELF electric-field exposure, however, strong pineal melatonin rhythms were reestablished. This effect appeared to be an "all-or-none" response to electric fields between approximately 2 and 130 kV/m [Wilson et al., 1986].

Indeed, an accumulating body of data suggests that ELF electric- and netic-field exposure can affect circadian rhythms and pineal function in s different species. The pineal glands of both pigeons and rats respond acut changes in the geomagnetic field [Olcese et al., 1988], and Welker et al. [showed that NAT activity and melatonin synthesis in pinealocyte cultur suppressed by weak ELF magnetic fields. Lerchl et al. [1990] demons marked changes in pineal serotonin metabolism in rats and mice expo intermittent magnetic fields at night, but no such changes were observe consequence of daytime exposure. Wever [1968] reported that expos 50-Hz electric or magnetic fields can act as a "zeitgeber," arresting the l ening of the circadian cycle that normally occurs when humans are depri temporal cues. However, we know of no direct experimental evidence th electromagnetic-field exposure can affect human pineal gland function.

We have completed a study to determine if domestic ELF electri magnetic-field exposure from using electric blankets could affect pineal tonin secretion in humans. Use of electric blankets represents a periodic sure to ELF fields that normally occurs at night when the pineal is most Exposure to electric blankets, as used in this study, did not require altera the normal lifestyle or daily routine of the subjects. To assess possible c in pineal melatonin secretion, we determined overnight urinary 6-hy melatonin sulfate (6-OHMS) excretion in healthy adult human voluntee

MATERIALS AND METHODS

Exposure Systems

Both conventional electric blankets and continuous polymer wire electric blankets were used. The heating element of CPW blankets co two parallel conductors separated by a resistive polymer material. Curre ing between the two conductors through the polymer is inversely prop to temperature at any point along the element. This feature eliminates t for the thermal safety switches used in conventional electric blankets vides some degree of auto temperature control. CPW blankets were cause they can be safely heated by either AC or DC power, allowing cor of AC and DC field effects. Our original assumption was that the DC-p blankets should have little or no effect on pineal gland function. (Aft studies were completed, however, Lerchl et al. [1990] showed that int DC magnetic fields can indeed affect pineal gland function in rats.) safety switches in the conventional electric blankets tested tended to a DC power at temperatures greater than about 140°F. This arcing const unacceptable fire hazard, and hence these blankets were deemed unsu use with DC power.

Modifications to the CPW blankets consisted of power supplies constructed in grounded metal boxes that could fit near, or under th the bed. AC and DC power supply boxes could not be distinguishec appearance or weight, and both types allowed use of the bedside ter controllers that the manufacturer supplied with the blankets. Blanket ture control units were dimly lit by an internal bulb that was the sam

Table 1. Measured Steady-State Magnetic Field Values[a] Generated at 10-cm Distance by Continuous Polymer Wire (CPW) Blanket in AC and DC Power Modes and by Conventional Electric Blanket in AC Power Mode

	Head	Chest	Knees
Background	0.78	0.89	0.84
Conventional	2.4	4.4	5.6
CPW (AC)[b]	4.2	6.6	5.6
CPW (DC)[b]	0.56	0.56	0.57

[a]Values are in milligauss (measured approximately 10 cm from blanket surface).
[b]Values were four to five times greater during warmup.

CPW and conventional electric blankets. When both husband and wife were participating in the study, a larger power supply was used to accommodate the individual temperature controllers for both sides of the bed. Subjects were not informed as to whether their blankets were powered by AC or DC at any given time. Nonfunctional (sham) power supply boxes were provided for use with the conventionally wired blankets.

Subjects

Volunteer subjects in the study consisted of 32 healthy, nonpregnant, premenopausal women and 10 healthy men. Male and female participants were randomly divided into three groups. Each of the groups provided early evening and morning urine samples for 2 weeks (period 1—preexposure) before beginning exposure. When exposure began, group 1 (n = 12 women, 2 men) slept nightly for 4 to 5 weeks (period 2) under AC-powered CPW blankets. Group 2 (n = 10 women, 4 men) used DC-powered blankets in the same manner. After 4 to 5 weeks of exposure, power modes on the blankets for groups 1 and 2 were switched, and exposure continued for an additional 4 to 5 weeks (period 3). Because of differences in the fields produced by AC-powered CPW and conventional electric blankets (Table 1), one group of 14 volunteers (group 3: n = 10 women, 4 men) used AC-powered, conventionally wired blankets for a total of 7 weeks of exposure. Urine samples were also collected from all three groups for 2 weeks (period 4) after cessation of exposure.

Because of the anticipated large variation in melatonin excretion among individuals, the study was designed so that volunteers would act as their own control. The study population was selected from residents of southeastern Washington State, a region centered around 46°15′ N latitude. At this latitude, winter solstice sunrise was at 0739 h and sunset at 1613 h. To control for possible changes in melatonin secretion arising from differences in the hours of daylight [Bojkowski and Arendt, 1988], study periods 1 and 2 were contiguous and ended just before the winter solstice. Periods 3 and 4 were contiguous and began just after the winter solstice. Because of the time required to change blanket power modes, there was essentially no break in exposure between periods 2 and 3.

The measure for assessing possible effects from ELF electromagnetic-field exposure was pineal gland function, as determined by radioimmunoassay (RIA) of urinary 6-OHMS. 6-OHMS is a stable metabolite of melatonin, and its levels in

urine reflect pineal melatonin secretion over time [Arendt, 1986]. The sample collection method did not allow gathering of information on possible temporal shifts in the melatonin peak that might occur in the time span between the last urine voiding before retiring and the first morning urination.

Volunteers provided a set of two samples, a late afternoon/early evening urine (generally around 1700 h) and the first morning void urine (generally between 0600 and 0700 h), three times each week during the study. Samples taken in the late afternoon/early evening were used as controls for the morning void urine, which was used to assess overnight melatonin excretion. Volunteers recorded the clock time of last urination before retiring (urine not retained), as well as that for the evening and morning urine samples. Samples were refrigerated by the volunteers immediately after collection, picked up three times per week, and processed in the lab within a few hours of pickup. Total urine volumes were measured and recorded; three sets of aliquots (5 ml each) were then taken, one for analysis by RIA, one for creatinine determination, and one to be held for archival purposes. In total, more than 2,400 primary urine samples were collected and analyzed by RIA. Levels of 6-OHMS were normalized to creatinine content and to urinary volume and time. Excreted melatonin levels were thus expressed as nanograms of 6-OHMS per milliliters urine/hour, or as nanograms of 6-OHMS per milligram of creatinine; the measures were essentially equivalent. Cretainine normalization yielded lower variance and was therefore used for further statistical analyses.

Assay for Urinary 6-Hydroxymelatonin Sulfate

Urinary 6-OHMS excretion was determined using an RIA kit supplied by CIDtech Research Inc. [Mississauga, Ontario, Canada]. The assay is a modification of that described by Arendt [1986] in which 6-OHMS is iodinated with ^{125}I using a method adapted from Vakkuri et al. [1984]. The iodinated material (suspended in methanol) was separated on cellulose F thin-layer chromatography plates using a butanol, water, and acetic acid solvent (4:1.5:1). Measurements in unknown samples were based on a standard curve using known amounts of 6-OHMS antigen (0–200 pg/ml) diluted in stripped urine. The effective working range for the assay (linear portion of the curve) was between 0.5 and 100 pg/ml. Within-assay variance among triplicate samples averaged 9.5%; between-assay variance was 14%. Samples were run in triplicate at two or three different dilutions. Daytime urines were diluted between 50:1 and 250:1 and nighttime urines between 2000:1 and 8000:1.

Statistical Analysis

Results of daytime and nighttime 6-OHMS measurements were compiled for each subject and for the three groups of subjects during the study. All statistical analyses were performed on overnight 6-OHMS measurements. Data for each group were analyzed separately because of the significant difference in the measured preexposure urinary 6-OHMS excretion of groups 1 and 2, and the delay in the start of exposure of group 3.

Nested analysis of variance was used to test the hypothesis that the 6-OHMS means of preexposure, AC exposure, DC exposure, and postexposure

periods are equal for each group [Winer, 1971]. A subject within-period error term was used to test this hypothesis. A natural logarithmic transformation of the data was made before the analyses to achieve homogeneity of variances. Data for each subject were analyzed independently by one-way analysis of variance to test the hypothesis that the 6-OHMS means of the four periods were equal for that subject. The measurement within-period error term was used to test the hypothesis. Differences among means were delineated using the least-significant-difference test [Fisher, 1949]. Again, a natural logarithmic transformation of the data was made before the analysis to achieve homogeneity of variances. Also, the nonparametric procedure known as the sign test [Siegel, 1956] was used to evaluate the direction of the differences between pairs of period means for each subject and for each group of subjects. All statistical hypotheses were tested at the 0.05 level of significance. The general linear model (GLM) procedure from Statistical Analysis System (SAS, 1985) was employed for analysis of variance.

Electric Blanket Magnetic and Electric Fields

Magnetic fields associated with the CPW and conventional electric blankets were measured on three orthogonal axes using a Deno[1] meter magnetic-field measuring device. The blankets were suspended from the ceiling for these measurements. Instrument probe design obviated making actual measurements closer than 10 cm from the blankets. Table 1 shows the steady-state magnetic fields measured for both types of blankets at the human head, torso, and knee regions. AC magnetic fields produced in the DC power mode were approximately an order of magnitude less than those measured in the AC mode and were not distinguishable from background.

Both the average and maximum magnetic fields associated with the CPW blankets in the AC mode are approximately 50% higher than those for comparably sized conventional electric blankets. Florig and Holburg [1990] have carried out detailed computer simulations of both the electric and magnetic fields associated with conventional and CPW blankets of several sizes. Data from their work are in general agreement with our measurements. At initial switch-on, the CPW blanket may draw as much as five times its steady-state current, and during this period produces a proportionally higher magnetic field. During steady-state operation the modified CPW blankets had a slightly higher current just after switch-on than just before switch-off. Blanket duty cycles were characterized at a room temperature of 23.5°C while the blankets were maintained at approximately 26.5°C. A current shunt and a data-logging device were used to record current draw. Current levels and the on-off cycle for a queen-size CPW blanket with one side operating are shown in Figure 1A. Comparable data from a conventional queen-size electric blanket are shown in Figure 1B.

RESULTS

Table 2 shows the group means and corresponding log-transformed data, pressed as nanograms of 6-OHMS/mg creatinine, for each exposure period.

[1]Deno is a registered trademark of Electric Field Measurements Co., West Stockbridge, MA.

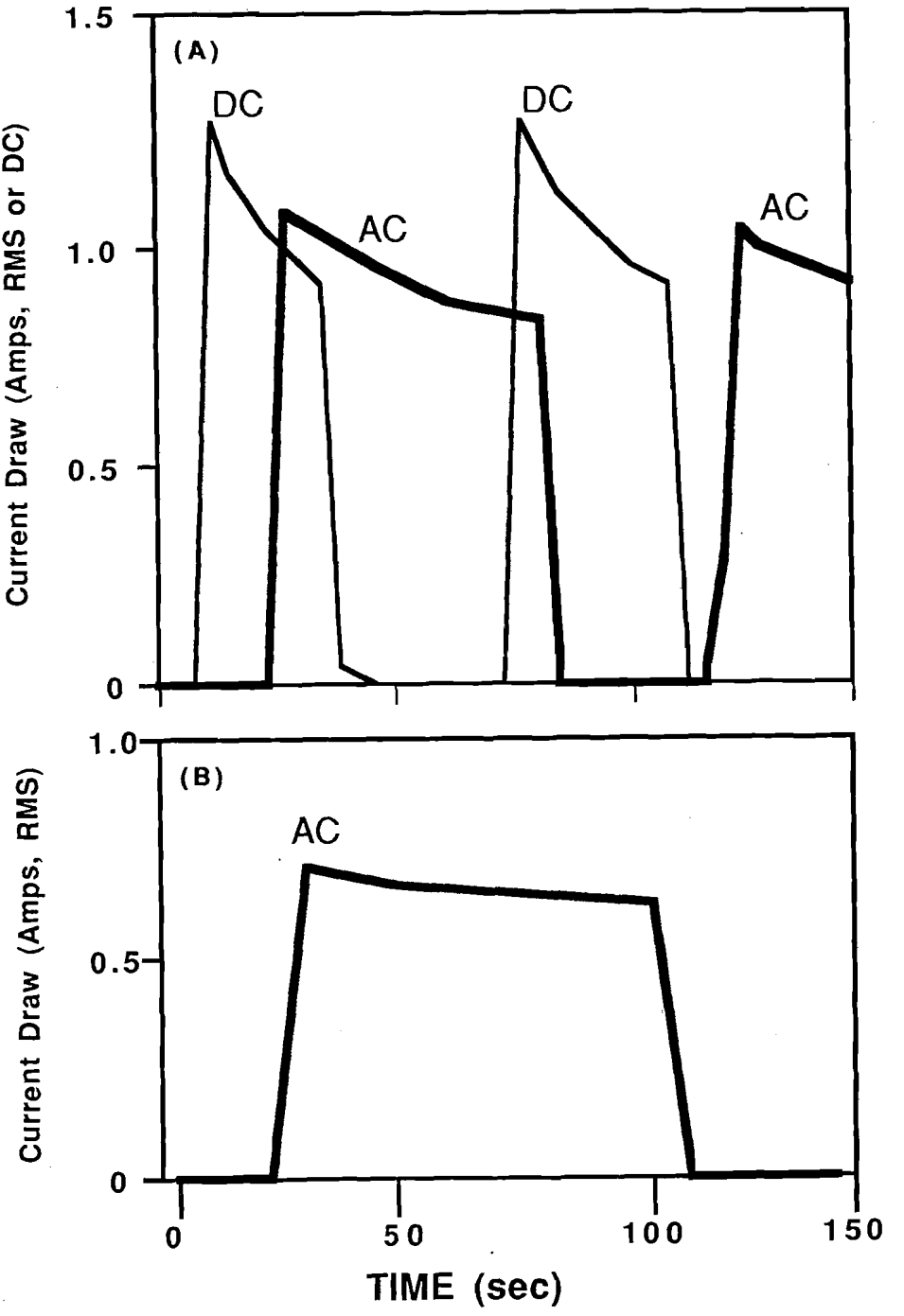

Fig. 1. (A) Plot of current draw during typical 150-sec interval for continuous polymer wire (CPW) electric blankets using AC power (thick line) and DC power (thin line). (B) Plot of current draw during 150-sec interval for conventional electric blanket using AC power.

Table 2. Group Means[a] for 6-Hydroxymelatonin Sulfate (6-OHMS) Excretion During Four Exposure Periods

	Exposure Period			
	1 (preexposure)	2	3	4 (postexposure)
		AC	DC	
Group 1 (CPW)	21.84 ± 3.74	23.46 ± 3.22	20.73 ± 3.41[b]	24.53 ± 3.26[b]
(n = 14)	2.88 ± 0.17[c]	2.92 ± 0.18	2.77 ± 0.18	3.01 ± 0.15
		DC	AC	
Group 2 (CPW)	14.13 ± 1.83	17.86 ± 2.10	13.97 ± 1.55	18.27 ± 2.89[b]
(n = 14)	2.49 ± 0.14	2.71 ± 0.13	2.48 ± 0.12	2.69 ± 0.16
		AC		
Group 3 (conventional)	18.89 ± 2.89	18.46 ± 2.95	——→	19.58 ± 3.49
(n = 14)	2.68 ± 0.21	2.60 ± 0.19	——→	2.68 ± 0.19

[a]± Values are standard error of the mean.
[b]Significantly different from previous exposure period by the sign test.
[c]Log-transformed (log e) values are listed beneath their respective means.

ere was no statistically significant difference in 6-OHMS excretion between AC and DC exposure periods as determined by analysis of variance of the group means. However, as determined by the nonparametric sign test, there was a significant difference in 6-OHMS excretion between periods 2 and 3, and between periods 3 and 4 in group 1, as well as between periods 3 and 4 in group 2.

Comparison of mean 6-OHMS excretion for individual subjects among the four test periods showed that seven CPW users (6 women and 1 man) had significant differences in the mean levels of 6-OHMS excretion as determined by analysis of variance. That is, there was a statistically significant difference between the levels of 6-OHMS excretion among at least two of the latter three test periods. Probabilities from analysis of variance on data for those individuals showing changes among exposure periods ranged between $P < 0.04$ and $P < 0.0001$.

Figure 2 is a plot of nightly 6-OHMS excretion from a CPW blanket user. Mean values for each exposure period are denoted by the height of the shaded area. There was a significant decrease ($P < 0.05$) during exposure period 3 as compared to exposure period 2 and a rebound to higher values after the cessation of exposure ($P < 0.05$). Six of the seven individuals exhibiting differences in 6-OHMS excretion showed this same pattern of melatonin excretion among the four exposure periods, as did the group 1 and group 2 populations in general (see Table 2).

Similar analysis of the conventional electric blanket data sets showed no such changes. Indeed, data from the conventional electric blanket users (group 3) showed no statistically significant changes among any of the exposure periods. As an additional check, we compared mean values before and after either 3 weeks of conventional electric blanket exposure. We found no significant individual or population changes by any of the foregoing criteria in group 3.

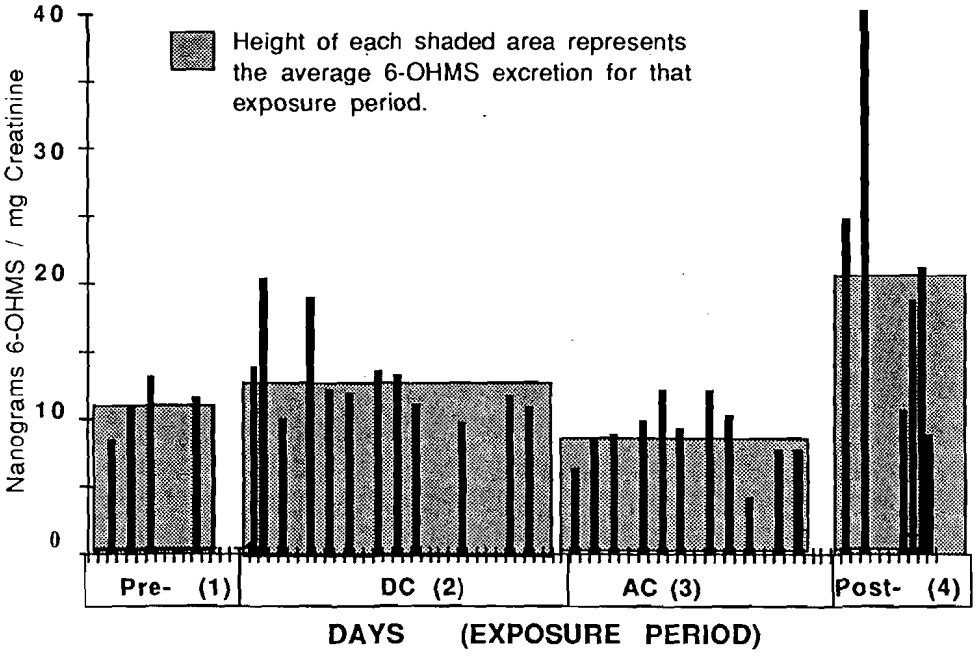

Fig. 2. Nightly 6-hydroxymelatonin sulfate (6-OHMS) excretion for continuous polymer wire blanket user. Height of shaded area represents period mean. Note increased 6-OHMS excretion immediately after onset and cessation of exposure.

DISCUSSION

Data on individual subjects serving as their own controls provided evidence to suggest that exposure to either or both intermittent DC, and 60-Hz AC, electric or magnetic fields of sufficient magnitude or duration may give rise to changes in melatonin excretion in some individuals. From the pattern of 6-OHMS excretion observed for those volunteers who showed a response to the fields, it appeared that there was a transient increase in 6-OHMS excretion in response to onset of exposure and a similar increase, of greater magnitude, at cessation of exposure.

During AC operation, the CPW blankets produced a magnetic field approximately 50% higher than did the conventional electric blankets. Owing to their duty cycle, CPW blankets switched on and off approximately twice as often as did the conventional blankets. Other possible factors that may have affected the outcome of the study include the combined effects of AC and DC exposure, differences in the switching transients of the two types of blankets, and the presence of operating shielded transformers in the bedrooms of the CPW volunteers. It is also possible that there were temporal shifts in the nighttime melatonin peak for the conventional electric blanket users that were not detected in the urinary 6-OHMS assay.

It should be noted that there was no group in the study wherein blanket heating was present without either an AC or a DC electric field. In the literature, however, we could find no evidence that warmth generated by a heated blanket has a physiological effect different from that achieved by using more or heavier

blankets. In addition, the conventional electric blanket users showed no changes in 6-OHMS levels, lending strength to the hypothesis that the electromagnetic fields associated with the CPW blankets, and not the heat that they generate, can affect human pineal function.

In further studies, it would be of interest to determine what, if any, physiological or genetic factors may be common to those individuals who exhibited change in 6-OHMS excretion as a consequence of electromagnetic field exposure. The report of McIntyre et al. [1990] cited earlier illustrated large variations in pineal gland sensitivity among individuals. Further work will be required to determine more precisely those electromagnetic-field characteristics that may be responsible for the observed changes in 6-OHMS excretion for certain individuals in the study.

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