Appendix Five

A Nested Case-Control Study of Residential and Personal Magnetic Field Measures and Miscarriages

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Magnetic Fields and Miscarriage

Word count abstract = 199

Word count text = 4,974

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*The views in this paper do not reflect an official position of the National Cancer Institute.

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A Nested Case-Control Study of Residential and Personal Magnetic Field Measures and Miscarriages

A nested case (n=177)-control (n=550) study was conducted to assess the relationship between clinical miscarriage and magnetic fields measured 30 weeks after conception. Also, a prospective sub-study of 219 participants of the same parent cohort was conducted to determine if prospective exposure results were similar to those found for the nested study. Residential estimates of fields from power lines (wirecodes), spot measures and three personal metrics, 1) the average difference between consecutive levels (a rate of change metric), 2) the maximum level and 3) the time weighed average were evaluated. Little association was found for wirecodes and spot measures. Adjusted odds ratios and 95% confidence intervals for the highest to the lowest quartile comparisons, using the 25^{th} percentile quartile as the reference group, were, respectively: 3.08, (1.59-5.95), 2.29 (1.19-4.40), and 1.53 (0.77-3.05) for the rate of change metric (trend p-value <0.001); 2.30 (1.21-4.36), 1.90 (1.00-3.51), and 1.44 (0.74-2.80) for the maximum value (trend p-value <0.001); and 1.68 (0.87-3.23), 1.74 (0.92-3.30), and 1.73 (0.91-3.26) for the time-weighted average (trend p-value 0.17). The prospective sub-study results were consistent with the nested study results. Future studies should confirm these findings and identify methods to reduced fields from sources of high, brief exposures.

Key words: miscarriages, spontaneous abortions, magnetic fields, electromagnetic fields, personal exposures, wirecodes

The initial concern about electric magnetic fields (EMFs) and miscarriage was prompted by reports of miscarriages among women who used video display terminals (VDT). Epidemiological studies of VDTs, overall, showed no association with miscarriages (see review papers 1,2). However, most of these studies did not assess EMF exposures. The results of two VDT studies (3,4) designed to assess VDTs as an EMF source was inconsistent. Only one of these two studies adequately defined high to low exposure groups (based on laboratory measures of the VDT) (4). This study found a clear dose-response. Women who used the VDT models with the highest measured magnetic fields had the highest risks (OR of 3.4, 95% C.I. of 1.4-8.6).

Several studies assessing electric bed heater use, assumed to be a source for strong magnetic fields, found positive associations (5-6). We conducted a study with equivocal findings (7). These and the VDT studies used surrogate measures to assess magnetic field exposures possibly resulting in lower risks due to random exposure misclassification.

Only one nested case-control study used magnetic field measurements to estimate a woman’s personal exposure (8). Although based on a small number of exposed women, they found that women with pre-clinical pregnancy loss were 5.1 times (95% C.I. of 1.0-25) more likely to have high front door measures than women who carried their pregnancies to term.

No study to date has directly measured personal EMF exposures. As a result, we added a nested case-control study using personal magnetic field (MF) measurements to a prospective study of 3,403 women assessing miscarriage and environmental factors. Cases consisted of all women who had a clinical miscarriage before 20 weeks gestation. Controls consisted of a random sample of women who had a live birth.

The hypotheses were that cases were more likely than controls to: 1) live near the type of power lines with a high enough current to potentially emit high magnetic field levels; 2) have higher residential magnetic field spot measures, assessed 30 weeks after conception; and 3) have higher personal (at home, at work, and outside the work and home environments) magnetic field exposures, assessed 30 weeks after conception.

Three personal magnetic field metrics were chosen *a priori:* 1) the time-weighted average (TWA) assessing the average mean value weighted over time, 2) a rate of change metric (RCM) assessing the absolute change in field levels between successive 10 second samples (see 9), and the maximum level (Max) assessing the highest value experienced. Although, the TWA has been the traditional metric in assessing exposure to power line frequency magnetic fields, in the absence of any mechanistic information the other two metrics are considered since they may capture different exposures than that reflected by the TWA.

We assumed that, by using a nested case-control design, cases and controls would be representing their respective underlying populations. Also, we assumed that magnetic fields measured at 30 weeks after conception (after the miscarriages occurred) would be similar to those experienced during the participant’s first trimester of pregnancy. To evaluate the second assumption, we conducted a prospective sub-study to determine if the associations found between miscarriages and personal magnetic fields obtained prospectively were similar to the nested case-control study results.

METHODS

Subject recruitment

Participants were selected from a cohort of 3,403 pregnant women in northern California who participated in a large prospective interview study designed to examine possible associations between miscarriages and various environmental factors. Eligible participants of this large prospective study were at least 18 years old, enrolled at 13 weeks gestation or less, Spanish or English speaking, and were members of the Kaiser Permanente Medical Care Program at the Fontana, the Santa Clara and the Walnut Creek medical facilities. Details of the parent prospective study population recruitment are described elsewhere (10). The participants for the case-control study and the prospective sub-study presented in this paper were recruited from the Santa Clara and Walnut Creek Kaiser Permanente facilities as shown in Figure 1.

For the prospective sub-study, a random sample of 531 participants from the parent prospective cohort was selected. On a weekly basis, women were recruited around one to two weeks after they completed their prospective study telephone interviews. Recruitment was between March 1990 and April 1991. Magnetic field measurements were obtained over two periods: around 12 weeks and then again around 30 weeks after conception. The latter was during the measurement period for the nested case-control study (described below). A total of 219 participants was recruited (201 eventual controls and 18 eventual cases). Of these, 176 (80%), 166 controls and 10 cases, participated in the second measurement period.

To identify subjects for the nested case-control study, pregnancy outcome was assessed around 25-30 weeks gestation by medical chart review. All 328 women with a reported miscarriages (cases) and a random sample of 806 women who were still pregnant at the time (non-cases, potential controls) were identified by sampling on a weekly basis between July, 1990 and November, 1991. About 51 percent (N=167) of the cases and 48 percent (N=384) of the non-cases eventually participated; prospective questionnaire data were available for the non-participants.

A total of 177 cases (51 percent, 177/(18+328)) and 550 controls (55 percent, 550/(201+806)) was in the nested case-control study, including those who also participated in the prospective sub-study. For this paper, only those participants who did not move between their first trimester of pregnancy and the time the measurements were obtained (155 cases and 509 controls) were included.

Pregnancy Outcome

All pregnancy outcomes were confirmed within a year of the participant's last menstrual period by: searching computerized hospital records (73 percent); abstracting medical records (18 percent); or follow-up telephone interviews, mailed questionnaires, or matches to California vital records (8 percent). Less than 1 percent (n=35) of the outcomes from the parent prospective study could not be determined.

Miscarriages were defined as pregnancies that ended at 20 weeks gestation or less. Multiple births were considered as a single pregnancy outcome in the analyses. Elective abortions, ectopic and molar pregnancies were excluded from analyses.

Interviews For the Entire Prospective Cohort

Women were interviewed by telephone during the first trimester of pregnancy (between 4 and 13 weeks of gestation, on average about 8 weeks). A standardized computer-assisted interview collected information about demographics, reproductive and medical history, potential confounders for miscarriages, and various environmental exposures. During the telephone call to schedule the later (nested case-control) measurement phase, it was determined if the participant had moved since her first trimester of pregnancy.

Residential power line assessment

The types of power lines and their proximity to the participants’ homes were evaluated and then classified into the Wertheimer and Leeper wire code categories (11). The four categories were: VHCC, very high current configuration (used to estimate the highest magnetic field levels); OHCC, ordinary high current configuration; OLCC, ordinary low current configuration; and BURIED, underground lines (used to estimate the lowest magnetic field levels). Up to three power lines within 150 feet from the participant’s resident were evaluated. For each line, the shortest distance from the line to the property line closest to the home was assessed using a measurement wheel or a line of site device for difficult terrain. For apartments, the distance was measured to the nearest boundary wall of the women's unit. The distance was calculated as the average of the three different distance measures. The power line associated with the highest wire code of was used as the resident's wire code.

Magnetic Field Measures

The EMDEX-C meter (calibrated to measure a frequency range of 40 to 800 Herz), set on a 10-second sampling rate, was used for both the personal and residential spot measurements. During measurements the meter was worn around the waist. For this paper, the magnetic field is the resultant field of the three orthogonal axes' root mean square levels. Neither the field worker nor the participant knew the field levels when measurements were obtained. The meter displayed military time used by the field worker and participant to record the start and stop times of a measurement (a new environment), as described below.

To obtain personal, 24-hour measurements, participants of the prospective sub-study wore the meter twice, first around 12-14 weeks gestation and then around 30 weeks gestation for controls and, on the average, around 22 weeks after their miscarriages for cases. Participants of the nested case-control study only wore the meter during the later measurement period. Overnight exposure in bed was obtained by having the participant place the meter in a pouch located midway on her side of the bed. While wearing the meter, the participant used an activity card to indicate when she was at home, at work, outside the home and work environments (other), in bed at night, and when the meter was not worn. She recorded the start time, as displayed on the meter when she entered a new environment (home, work, or outside home and work). The participants were instructed not to alter their usual activity routine and to wear the meter as much as possible.

For the analyses, personal exposure was partitioned into: home (not in bed); bed (overnight bedroom exposure while sleeping); total home (home plus overnight bed exposure); other (not in the home or work environments); work; and total 24-hour (the total 24-hour exposure period). The calculations excluded the readings from the times the meter was not worn.

Front door measurements of one-minute were obtained during both the prospective sub-study and nested case-control study measurement periods. Residential magnetic field area measures were obtained only during the nested case-control study. One-minute readings were taken in the center of the kitchen, living room, and bedroom. The same meter that was used to measure the participant's personal exposure was also used to assess her residential spot measures the day after she wore the meter.

Statistical analyses

For the nested case-control study, cases were compared to controls with respect to: 1) residential wire codes; 2) average residential front door spot measures; 3) average residential inside spot measures; and 4) personal 24-hour magnetic field measures, partitioned into those exposures received in bed while sleeping, at home awake, at work and away from the work and home environments (other). For these, the odds ratios associated with high magnetic field levels or wire code classification were assessed. Potential confounders and modifiers of the odds ratios were assessed first by stratified analysis. For this the exposure was dichotomized into magnetic field levels above and below a defined cut-point. For wire code, each of the overhead wire code categories was compared to the buried category. For the residential spot measurements and personal TWA measures, a cut-point of 2.0 milligauss was used. This was the cut-point used for previously published childhood cancer studies (16). For the personal RCM and maximum values, the 50^{th} percentile cut point was used since the cumulative distributions of cases were higher than that found for controls at all exposure levels (see figures 3-5). For those variables where the odds ratios were homogeneous across strata, Mantel-Haenszel (17) analysis was used to calculate adjusted odds ratios for the assessment of confounding.

Multiple logistic regression was used to assess the independent associations between magnetic field measurements and wire codes and miscarriages. Covariates initially considered were: maternal age, gestation at the time of the prospective study phone interview (gestation at interview), prior fetal loss, nausea, race, income, education, body mass index, physical activity, perception of health, cigarette consumption at conception, alcohol consumption at conception, coffee and caffeine consumption at conception, season of magnetic field measurement, and Kaiser Permanente Medical Care Program facility. Variables included in the final logistic regression models were those variables that produced a 10% change in the odds ratio after the Mantel-Haenszel adjustment. For the personal magnetic field measure models, the variables included were those that changed the odds ratio for at least one of the 24-hour environments. The final model used miscarriage as the dependent variable, and the magnetic field exposures (wire codes, area measures, and personal measures) as the independent variable. The covariates were maternal age, coffee consumption at conception, income, race, and gestation at interview. The total home, work, and other personal measure environments were also adjusted for each of the other two environments.

Multiple logistic regression analyses were used to evaluate effect modification between high magnetic field exposures (including high wire code) and gestation at interview, income, race, and house type. No effect modification was found.

To evaluate a dose-response, risk was assessed within quartile exposure categories for each of the personal metrics. The three upper exposure quartiles were compared to the lowest exposure quartile (the reference group).

For the prospective sub-study, the denominator for calculating rates of miscarriages included all live births, miscarriages, and stillbirths. Miscarriage rates for women in environments with higher than usual magnetic fields were compared with those of women in environments with lower than usual magnetic fields for wire codes, personal TWA, personal RCM and personal maximum levels (Max). Initially we compared persons living in VHCC wire code homes to those living in BURIED wire code homes and persons with personal metrics levels above the group 50th percentile value to those with measures below this value. For the TWA metric, an additional assessment was done for a cut point of 2.0 milligauss.

RESULTS

Nested participants versus non-participants

Table 1 compares the adjusted odds ratios and 95% confidence intervals of the relationship between various important variables and miscarriages for the northern California prospective study participants with the nested case-controls study participants. The participants of the nested case-control study basically represent the larger parent cohort since the overall results were similar between the two study groups.

Nested study cases versus controls

Table 2 summarizes the main characteristics that differ between cases and controls. Compared to controls, cases were more likely to be older, to be interviewed earlier in gestation, to be categorized as a race other than white and Hispanic, not to consume cigarettes around conception, to have a household income of $50,000 or more, to reside in a single family home, and to not experience nausea during their first trimester of pregnancy. The distributions of wire code, education, body mass index around conception, perception of health, physical activity, season of the magnetic field measurement, Kaiser Permanente Medical Program, and the known risk factors of prior fetal loss, and alcohol, and coffee consumption around conception were similar between cases and controls.

Inter-correlation of the nested study magnetic field exposure estimates

Four different magnetic field exposure estimates (wire code, personal time-weighted average (TWA), personal average rate of change metric (RCM) and personal maximum (Max) value were compared between cases and controls based on the assumption that they captured different aspects of a person's magnetic field exposure. As shown in Figures 5-7, this assumption seems reasonable for the personal measurements and wirecodes. Both the RCM (Figure 6.) and maximum value (Figure 7.) total home exposures were not related to wire codes while the TWA (Figure 5.) measurements were modestly related. While 8.5% of all women had personal home TWAs above 2 mG only 5.8% of women living next to underground lines had personal home readings this high (p=.04). The personal metrics were correlated with each other, but not strongly. The highest correlation was between the maximum value and the RCM measure (Table 3).

Wirecodes and miscarriages risk

Only participants' first trimester homes were categorized into wirecode classifications. Cases were 1.2 (0.7-2.1) times more likely than controls to live in VHCC homes, but this association was not statistically significant. Cases and controls were equally likely to live in OHCC and OLCC homes. The results were similar even after adjusting for maternal age, gestation at interview, coffee consumption at conception, income, and race (Table 4).

To evaluate if recruitment into the study was associated with wire code category, wire code assessment was obtained for the first trimester homes of 77% of the non-participant cases and a 15% random sample of the non-participant controls. Unlike the participants, non-participant cases compared to non-participant controls were less likely to live in any of the overhead wire code homes, in particular, VHCC homes (OR of 0.48, 95% CI of 0.22-1.05). A selection bias may have led to the increased odds ratio for participants residing in the VHCC wire code homes. Even with this selection bias, the over all pattern indicated that wire codes were not significantly associated with miscarriages.

Residential spot measurements and personal time weighted average and miscarriage risk

The distributions of personal magnetic field TWA for the total 24-hour measurement period, each of its environments and the residential magnetic field spot measures were similar between cases and controls. As seen in Figure 2, the cumulative distributions of the personal 24-hour TWA for cases and controls were similar over the whole range of exposure. Table 5 shows the crude and adjusted odds ratios for each of the personal magnetic field TWA 24-hour environments and the magnetic field residential spot measures along with the median time each participant spent in each environment. Cases and controls did not differ with respect to the time spent in each of the personal 24-hour environments. For both the magnetic field personal and residential measures, a cut-point of 2.0 milligauss was used to distinguish between high and low exposures. Cases were slightly less likely than controls to have personal TWA exposures above 2.0 milligauss for the overnight bed, total home, other, and work environments. The observed decreases were not significant. Cases were slightly more likely than controls to have residential front door measures and personal home TWA exposures above 2.0 milligauss. These increases were also not significant. Cases and controls were similar with respect to their residential, inside spot measurements and their personal total 24-hour exposures.

To evaluate a possible personal 24-hour TWA dose-response, table 6 compares the crude and adjusted odds ratios and 95% confidence intervals by personal 24-hour exposure quartiles, using measures below the 25^{th} percentile value as the exposure reference group. For both the crude and adjusted odds ratios, a trend of progressively higher odds ratios with higher TWA quartiles was not observed. However, a modest step function was observed; cases were about 1.7 (0.9-3.3) times more likely than controls to have a personal total 24-hour TWA exposure above 0.72 milligauss (the 25^{th} percentile value).

Table 7 shows the adjusted odds ratios and 95% confidence intervals for having personal exposures greater than the 50th percentile value in at least two environments and in one environment compared to having exposures below this value in all environments. A trend was observed such that the highest odds ratio was found for those women who had greater than the 50th percentile TWA exposures in at least two environments (OR of 2.19, 95% CI of 1.18-4.05).

Average Change Metric (RCM) Levels and Miscarriage Risk

The distributions of personal magnetic field RCM for the total 24-hour measurement period and each of the locations were higher for cases compared to controls. Figure 3 shows higher personal 24-hour RCM levels for cases compared to controls over the entire range of exposure. As shown in Table 6, and unlike the personal TWA results, we observed a trend for progressively higher crude and adjusted odds ratios with higher RCM quartiles, using measures below the 25th percentile value as the reference exposure. Adjusted odds ratios and 95% confidence intervals for the highest quartile in comparison to the lowest quartile, respectively, were 3.08 who had (1.59-5.95); 2.96 (1.00-8.74); 1.75 (0.07-4.52). This increase was slightly more pronounced for women who had earlier miscarriages.

As with the TWA, a gradient in miscarriage risk was observed as the number of environments with exposures at or above the 50th percentile level increased. Adjusted odds ratio and 95%

confidence interval for women who had RCM levels above the 50 percentile value in at least two environments, compared to those with all environments with exposures below the 25 percentile value, was 2.38 (1.24-4.59) (Table 7).

Maximum Value Metric and Miscarriage Risk

Like the personal RCM results, the distributions of personal magnetic field maximum levels for the total 24-hour measurement period and each of its environments were higher for cases compared to controls. Figure 4 shows higher personal 24-hour maximum levels for cases compared to controls over the entire range of exposures. Also, like the personal RCM results, a trend was observed of progressively higher crude and adjusted odds ratios for higher maximum value quartiles, using exposures below the 25th percentile value as the reference exposure (see Table 6). Adjusted odds ratios and 95% confidence intervals for the highest to the lowest quartile comparisons, respectively, were 2.30 (1.21-3.83); 1.90 (1.00-3.51); and 1.44 (0.74-2.80). Like both the personal TWA and RCM results, this increased risk was more pronounced for women who had earlier miscarriages.

Like both the TWA and RCM results, a gradient in miscarriage risk was observed as the number of environments with exposures at or above the 50th percentile level increased. Adjusted odds ratio and 95% confidence interval for women who had RCM levels at above the 50 percentile value in at least two environments, compared to those with all environments with exposures below the 25 percentile value, was 1.99 (1.29-3.07) (Table 7).

Prospective sub-study results

As with the nested study results, there was no clear association found between wire code and miscarriage (Table 8). Also, women with personal total 24-hour magnetic field exposure at or above the 50^{th} percentile cut-point value for the RCM and the maximum value and at or above 2.0 milligauss for the TWA metric were about 2 times more likely to have a miscarriage than those women with personal exposures below these values. Although these increased risks were not significant due to the small sample size, they were consistent with the nested study results.

However, unlike the nested study results, the personal home, total home and other TWA magnetic field exposures above 2.0 milliguass were positively associated with miscarriages. (see Table 8). These results, assessed early during the analysis phase, prompted the funding of a prospective study that, recently, has been completed (14).

DISCUSSION

Personal magnetic field maximum exposures and/or exposures with large average differences between consecutive levels (the RCM) are associated with the risk of clinical miscarriages. For both these metrics a dose-response was observed with an increase in exposure and with the number of daily environments with exposures above the 50th percentile level. The TWA personal metric only demonstrated a slight non-significant increase in risk.

There are a number of strengths with this study. First, among studies of the relationship of miscarriage and exposures to electric and magnetic fields, this study is the first to evaluate personal magnetic field exposures for three different *a priori* summary metrics and for different types of daily environments (at home, at work, and outside the work and home environment). Previous studies have only assessed indirect or surrogate exposure estimates such as residential wire codes and self-reported use of electrical devices (1,2,5-7). These surrogate measures may not reflect a person’s exposure to magnetic fields.

Secondly, the effect of selection bias could be evaluated since the study was nested within a prospective pregnancy study. Overall, selection bias appeared to be minimal except perhaps for the wire code results. Regardless, the associated odds ratio for the highest wirecode category, VHCC, was only slightly greater than 1.0 with a large confidence interval including 1.0. Also, differential participation as a function of wire code status would not have produced the increased risks observed for the personal magnetic field maximum values and RCM levels since these metrics were not associated with wire code (see Figures 6-7) and wire code was not strongly associated with miscarriages.

Thirdly, the study was large enough to assess all the known risk factors of miscarriages for confounding and effect modification, including physical activity, a variable thought to be associated with changing or maximum field levels (Dan Bracken, personal communication). We found little or no confounding as well as effect modification. Also, we found that physical activity was not associated with any of the personal magnetic field metrics or miscarriages (15).

Finally, we compared the associations found for the nested study, using retrospective measures, with that found for a small prospective sub-study where personal exposures were obtained prospectively. The prospective sub-study personal measurement results, although slightly different than that found for the nested case-control study, nonetheless were consistent with the overall direction of the nested study results.

There are two main limitations to the study. First, as discussed above, the magnetic field measurements were obtained months after the first trimester and the occurrence of the miscarriages. Perhaps the behavior and magnetic fields of women who had a miscarriage were different from the very pregnant controls. The coherence of the results between the nested case-control study and the prospective sub-study argues somewhat against this. We found that the correlation between early and later personal measurements was moderate to poor, but this should be cautiously interpreted since repeated measures were conducted only for a small sample of women consisting of only 10 women with a miscarriage.

And secondly, we obtained personal magnetic field measures for only 50% of the parent cohort participants who were recruited for the nested case-control study. This could result in selection bias if participation was differential with respect to exposure status. While there was evidence of only a weak selection bias with respect to wire code, we cannot rule out the possibility of a selection bias for the personal RCM and maximum levels. However this would require that subjects would be aware of sources of brief high fields and that cases and controls would differentially enter the study on the basis of this exposure. The coherent results of the prospective study argue somewhat against this.

These findings are inconsistent with the results of published papers. Mechanistic and animal studies predominantly do not support an association of electric and magnetic fields and miscarriages (16). A number of laboratory studies have reported alterations in the development of chick embryos exposed to EMF (17-20).

Also, the nested study results are inconsistent with the results of our electric blanket and miscarriage study where we found that, overall, a decreased risk of miscarriages was associated with electric blanket use during the first trimester of pregnancy (7). The participants of both studies were derived from the same parent, prospective cohort. In this study we found higher than background RCM levels for electric blankets that were on during the night regardless of blanket setting. This was mainly for locations directly under (i.e. body surface position) to 10 cm under the blanket (i.e. uterus position). RCM levels were similar to background levels for areas 10 cm away for the edge of the blanket (i.e. retina position). Given this, and the findings of the nested study, one would expect that reported use of electric blankets during the first trimester of pregnancy would be positively associated with miscarriages, especially if the target organ for exposure was the uterus. If the target organ for exposure were the retina, we would expect no association of miscarriage among electric blanket users. Perhaps the inconsistency is due to the fact that the majority of electric blanket users kept their blankets on low settings for most of the night and at this setting, blankets may not have cycled (or stopped cycling) thereby emitting no or little magnetic fields. Hence, reported use of electric blankets may not reflect high nighttime exposure to magnetic fields.

And finally, the nested study results for the magnetic field front door spot measures are inconsistent with the findings of Juutilainen and coworkers (8) where they found a 5 fold increased risk of pre-clinical miscarriages among women who had front door measures above 3.0 mG. Perhaps risk of magnetic fields spot measures are easier to detect for unrecognized miscarriages than recognized miscarriages; our study only assessed clinically recognized miscarriages. Or, perhaps front door measures taken closer to the critical exposure period reflect a woman's first trimester magnetic field exposure more so than measures obtained some time after this. This is a possibility since the prospective sub-study's front door spot measurement results were somewhat consistent with the findings of Juutilainen and coworkers.

The personal magnetic field RCM and maximum values were lowest for overnight periods and highest for work environments. High RCM values and maximum levels were not associated with proximity to power lines, which we assessed through the wire code. Interestingly, there are no published studies to date that have quantified the sources for these types of brief high exposures.

About 75% of our participants experienced a personal maximum field exposure above 14 mG or an average change in fields (RCM) above 0.42 mG at least once during the 24-hour measurement period. An odds ratio of about 2.0 mG was found for these metric values or higher. Hence, if these exposures are causal, they could account four about 30% of the background rate of miscarriages. If these metric values were lowered to below the 25th percentile levels, the rate of miscarriage in our study would be reduced from 10% to 7%. A gradual increase in the rate of clinically recognized miscarriages from 7% to 10% with an increase in electricity use through the years may not have been detected. This is because miscarriages are not routinely monitored, an increase in exposure would have only gradually occurred in any one location overtime and there has been a concomitant increase in improved prenatal care overtime.

The preliminary TWA results of the prospective sub-study impelled the California Electric and Magnetic Fields Program to fund a prospective study of personal magnetic field exposure and miscarriage. The results of that study by Li et al are reported elsewhere (20). Interestingly, the authors analyzed the full range of exposure to Maximum magnetic fields and found an association with miscarriage above the 25th percentile. We had not picked this up in our preliminary analyses. Thus the findings reported here in data collected in the early 1990s serve as a confirmation of the results of Li et al.

ACKNOWLEDGEMENTS

This study was funded by the State of California. We acknowledge the critical comments from our scientific advisory panel: Doctors A. Afifi, M. Criqui, L. Sever, and N. Wertheimer. We also acknowledge, project coordinator, Dawn Duane, database manager, Soora Wi, field workers, Jeff Fisch, Christianna Williams, James Harding, Bonnie Faigeles, Amanda Ettinger, and Thomas Tarshis, and Myra Alcaide for manuscript preparation.

REFERENCES:

1. Shaw GM. Human adverse reproductive outcomes and electromagnetic fields: a brief summary of the epidemiologic literature. Bioelectromagnetics 2000; in press.
2. Delpizzo V. Epidemiological studies of work with video display terminals and adverse pregnancy outcomes (1984-1992). American Journal of Industrial Medicine 1994;26:456-480.
3. Schnorr TM, Grajewski BA, Hornung RW, Thun MJ, Egeland GM, Murray WE, Conover DL, Halperin WE. Video display terminals and the risk of spontaneous abortion. New Engl J Med 1991;324:727-33.
4. Lindbohm M-L, Hietanen M, Kyyronen P, Sallmen M, von Nandelstadh P, Taskinen H, Pekkanen M, Ylikoski m, Hemminki K. Magnetic fields of video display terminals and spontaneous abortion. Am J Epidemiol 1992;136:1041-51.
5. Wertheimer N, Leeper E. Possible effects of electric blankets and heated waterbeds on fetal development. Bioelectromagnetics 1986;7:13-22.
6. Belanger K, Leaderer B, Hellenbrand K, Holford TR, McSharry J, Power ME, Bracken MB. Spontaneous abortion and exposure to electric blankets and heated water beds. Epidemiology 1998;9:36-42.

7. Lee GM, Neutra RR, Hristova L, Yost M, Hiatt RA. The use of electric bed heaters and the risk of clinically recognized spontaneous abortions. Epidemiology 2000; 11: 406-415.
8. Juutilainen J, Matilainen P, Saarikoski s, Laara E, Suonio S. Early pregnancy loss and exposure to 50-Hz magnetic fields. Bioelectromagnetics 1993;14:229-236.
9. Wilson BW, Lee GM, Yost MG, Davis KC, Heimbigner T, Buschbom RL. Magnetic field characteristics of electric bed-heating devices. Bioeletromagnetics 1996; 17:174-179.
10. Swan SH, Waller K, Hopkins B, Windham GC, Fenster L, Schaefer C, Neutra RR. A prospective study of spontaneous abortion: relation to amount and source of drinking water consumed in early pregnancy. Epidemiology 1998;9:126-133.
11. Wertheimer N, Leeper E. Adult cancer related to electrical wires near the home. Int J Epidemiol 1982;11:345-355.
12. Savitz DA, Wachtel H, Barnes FA, John EM, Tvrdik JG. Case-control study of childhood cancer and exposure to 60-Hz magnetic fields. Am J Epidemiol 1988;128:21-38.
13. Breslow NE, Day NE, eds. Statistical methods in cancer research. Vol 1. The analysis of case-control studies. Lyon:International Agency for Research on Cancer, 1980. (IARC scientific publication no. 32).

14. Eskenazi B, Fenster L, Wight S, English P, Windham GC, Swan SH. Physical exertion as a risk factor for spontaneous abortion. Epidemiology 1994;5:6-13.

15. Portier, C and Wolfe MS Eds. Assessment of Health effects from Exposure to Power-Line Frequency Electric and Magnetic Fields: Working Group Report NIEHS 1998

16. Delgado JMR, Leal J, Monteagudo JL and Garcia MG. Embryological changes induced by weak, extremely low frequency electromagnetic fields. Journal of Anatomy 1982;134:533-551.

17. Juutilaiinen J, Saaili K. Development of chick embryos in 1 Hz to 100 kHz magnetic fields. Radiat Environ Biophys 1986;25:135-140.

18. Pafkova H, Jerabek J. Interaction of MF 50 hz, 20 mT with high dose of X-rays: evaluation of embryotoxicity in chick embryos. Reviews on Environmental Health 1994;10:235-241.

19. Farrell JM, Litovitz TL, Penafiel M, Montrose CJ, Doinov P, Barber M, Brown KM, Litovitz TA. The effect of pulsed and sinusoidal magnetic fields on the morphology of developing chick embryos. Bioelectromagnetics 1997;18:431-438.

20. Li, KD, Oudouli R, Wi S, Janevic T, Goditch I, Bracken D, Rankin R, Iriye R. A population-based prospective cohort study of personal exposure to magnetic fields during

pregnancy and the risk of spontaneous abortion. Submitted NEJM 2000.

TABLE 1. Comparison of Adjusted* Odd Ratios (OR) and 95% Confidence Interval (CI) for Miscarriage and Important Variables between Nested Case-Control Participants and the Parent Northern California Prospective Cohort.

		Prospective Cohort N = 3403	**Nested Cohort N = 664**
Variable*		OR (95% CI)	OR (95% CI)
Maternal Age (years)	<35, 35+	1.85 (1.10 - 3.05)	2.25 (1.62 - 3.12)
Gestation at interview (week)	<8, 8+	1.02 (.68 - 1.54)	1.35 (1.05 - 1.75)
Prior Fetal Loss	No, Yes	0.87 (.54 - 1.39)	1.07 (0.79 - 1.44)
Race 1	Other vs. White	2.08 (1.11 - 3.92)	1.42 (1.02 - 1.97)
Race 2	Hispanic vs. White	0.94 (.47 - 1.86)	1.00 (0.66 - 1.51)
Cigarette Consumption at LMP	No, Yes	0.71 (.39 - 1.29)	1.11 (0.79 - 1.55)
Alcohol Consumption at LMP	No, Yes	0.73 (.47 - 1.14)	0.87 (0.66 - 1.14)
Coffee Consumption at LMP	No, Yes	1.19 (0.74 - 1.91)	1.19 (0.89 - 1.61)
Body Mass Index 1	Thin vs. Avg	1.08 (0.66 - 1.75)	1.03 (0.77 - 1.38)
Body Mass Index 2	Heavy vs. Avg	0.84 (0.49 - 1.44)	0.83 (0.59 - 1.18)
Income	<$50,000, $50,000+	0.79 (0.49 - 1.77)	0.95 (0.72 - 1.24)
House Type**	Single vs. Other	0.93 (0.49 - 1.77)	0.74 (0.53 - 1.05)
Wire Code **	Vhcc vs. Other	1.24 (0.71 - 2.19)	1.02 (0.66 - 1.56)

* Adjusted for all other variables excluding house type and wire code.

** Information about house type and wire code was obtained for all of the nested participants but only for a 15% random sample of the prospective cohort; adjusted for all other variables including house type and wire code.

Abbreviation: N = number, LMP = last menstrual period.

TABLE 2. Comparison of Variables that are Different Between Cases and Controls **.

Variable*	**Case**		**Control**		
	N	%	N	%	p-value
Maternal Age (years)					
< 30	121	78.1	438	86.1	0.02
35+	34	21.9	71	13.9	
Gestation at interview(weeks)					
up to 6	49	31.6	141	27.7	0.04
6 - <10	92	59.4	280	55.0	
10+	14	9.0	88	17.3	
Race					
White	114	73.4	402	79.0	0.00
Hispanic	13	8.4	67	13.2	
Other	28	18.1	40	7.8	
Cigarette Consumption Around Conception					
No	137	88.4	414	81.3	0.04
Yes	18	11.6	95	18.7	
Income					
< $50,000	35	22.9	147	29.2	0.13
$50,000 +	118	77.1	356	70.8	
House Type					
Single Family Home	116	74.8	335	65.8	0.05
Apartment	20	12.9	109	21.4	
Other	19	12.3	65	12.8	
Nausea During First Trimester					
Yes	99	63.9	415	81.5	0.00
No	56	36.1	94	18.5	

* Numbers of some variables do not total because of missing data.
** Cases and controls who did not move since their first trimester.
Abbreviation: N = number, % = percent.

TABLE 3. Person's Correlation Coefficients (r) Comparing the Relatedness of the Three Personal Magnetic Field Total 24-hour Exposure Metrics for Nested Participants.

Metric Comparison	r N=614
LogTWA vs. LogMax	0.44
LogTWA vs. RCM	0.49
LogMax vs. RCM	0.62
TWA vs Max	0.86
TWA vs RCM	0.78
Max vs RCM	0.96

Abbreviations: TWA = time weighted average, Max = maximum value, RCM = rate of change metric, Log TWA = log of the time-weighted average, LogMax = log of the maximum field value, N = number.

Table 4. Odd Ratios (OR) and 95% Confidence Interval (CI) for the Association Between Miscarriages and Wire Code Category.

	Participants*				Non-Participants*			
Wircode	N	%	Crude OR (95% CI)	Adjusted** OR (95% CI)	N	%	Crude OR (95% CI)	Het.*** p-value
Vhcc								
Case	26	15.2	1.21 (0.71-2.07)	1.27 (0.74-2.20)	9	7.4	0.48 (0.22-1.05)	0.05
Control	68	12.6			48	12.1		
Ohcc								
Case	35	20.5	0.87 (0.55-1.40)	0.94 (0.58-1.51)	23	18.6	0.72 (0.41-1.24)	0.59
Control	127	23.4			82	20.7		
Olcc								
Case	46	26.9	1.01 (0.66-1.57)	1.01 (0.65-1.57)	32	25.8	0.72 (0.44-1.18)	0.32
Control	144	26.8			113	28.5		
Buried								
Case	64	37.4	1.00	1.00	60	48.4	1.00	
Control	203	37.5			153	38.6		

* For first trimester homes only.
** Adjusted for maternal age, gestation at interview, coffee consumption at conception, income, and race.
*** Chi-square for heterogeneity p-value comparing nested participants to non-participants.
Abbreviations: N = number, % = percent.

Table 5. Odd Ratios (OR) and 95% Confidence Interval (CI) of Magnetic Field Personal Time-Weighted Average and Average Home Spot Measures by Area Location.

	N	Median Time (hours)	% Above 2.0 mG	Crude OR (95% CI)	Adjusted**OR (95% CI)
Bed					
Cases	136	8.8	5.9	0.71 (0.32-1.55)	0.62 (0.20-1.95)
Controls	494	9.0	8.1		
Home					
Cases	131	6.0	7.6	0.99 (0.56-1.76)	1.42 (0.51-4.00)
Controls	481	7.0	7.7		
Total Home					
Cases	131	14.7	5.3	0.58 (0.25-1.31)	0.84 (0.20-3.54)
Controls	482	16.6	8.9		
Other					
Cases	127	2.7	7.9	0.88 (0.43-1.81)	0.87 (0.29-2.61)
Controls	440	2.5	8.9		
Work					
Cases	82	7.6	17.1	0.8 (0.42-1.54)	0.71 (0.33-1.51)
Controls	239	7.6	20.5		
Total 24-hour					
Cases	131	23.3	9.9	1.02 (0.54-1.95)	0.97 (0.45-2.10)
Controls	483	23.2	9.7		
Front Door Spot					
Cases	155	1 minute	9.1	1.28 (0.67-2.45)	1.22 (0.60-2.49)
Controls	501	1 minute	7.2		
Inside Spots					
Cases	155	4 minutes	7.7	1.33 (0.66-2.67)	1.05 (0.51-2.19)
Controls	506	4 minutes	5.9		

*Nested Participants who reside in their first trimester house at the time of measurements.
**Adjusted for: maternal age, gestation at interview, coffee consumption around conception, income, race, and area location.
Abbreviation: N = number, % = percent, mG = milligauss.
Cutpoint = 2.0 milligauss.

Table 6. Odds Ratio (OR) and 95% Confidence Interval (CI) of the Association Between Total 24-hour Personal Magnetic Field Time Weighted-Average (TWA), Rate of Change Metric (RCM), Maximum (Max.) Value and Miscarriage by Quartiles.

Time Weighted Average (mG)					
TWA Value		**Number**	**Percent**	**Crude OR (95% CI)**	**Adjusted OR* (95% CI)**
1.28 +	Case	35	26.7	1.59 (0.89-2.84)	1.68 (0.87-3.23)
	Control	123	25.5		
0.93-<1.28	Case	37	28.2	1.75 (0.98-3.12)	1.74 (0.92-3.30
	Control	114	23.6		
0.72-<0.93	Case	36	27.5	1.53 (0.86-2.75)	1.73 (0.91-3.26)
	Control	122	25.3		
< 0.72	Case	23	17.6	1.00	1.00
	Control	124	25.7		
			χ2Trend p-value	0.17	
Rate Change Metric (mG)					
RCM Value					
0.94+	Case	46	35.1	3.25 (1.76-6.00)	3.08 (1.59-5.95)
	Control	109	22.5		
0.62-<0.94	Case	37	28.2	2.42 (1.29-4.52)	2.29 (1.19-4.40)
	Control	118	24.4		
0.43-<0.62	Case	31	23.7	1.90 (1.0-3.60)	1.53 (0.768-3.05)
	Control	126	26.0		
<0.43	Case	17	13.0	1.00	1.00
	Control	131	23.8		
			χ2Trend p-value	0.00	
Maximum Value (mG)					
Max Value					
35.05+	Case	39	29.8	2.13 (1.18-3.83)	2.30 (1.21-4.36)
	Control	115	23.8		
23.42-<35.05	Case	38	29.0	2.08 (1.15-3.37)	1.90 (1.00-3.51)
	Control	115	23.8		
14.31-<23.43	Case	33	25.2	1.71 (0.94-3.12)	1.44 (0.74-2.80)
	Control	121	25.1		
<14.31	Case	21	16.0	1.00	1.00

Control	132	23.8	
		χ^2Trend	
		p-value	0.00

* Adjusted for: maternal age, interview at gestation, coffee consumption at conception, income, and race.
*** mG between 10 second samples.
Abbreviations: mG = milligauss.

Table 7. Crude and Adjusted Odds Ratio (OR) and 95% Confidence Intervals (C.I.) of Miscarriage and Personal Magnetic Field Exposure by Number of Area Location at or above the 50th percentile Cutpoint Exposure Value by Exposure Metric.

	Max Value (cutpoint=23.43)				RCM Value (cutpoint=0.62)				TWA (cutpoint=0.93)			
	N	**%**		**OR (95% C.I.)**	**N**	**%**		**OR (95% C.I.)**	**N**	**%**		**OR (95% C.I.)**
At or Above in Any Two Environments												
Case	23	17.6%	Crude	3.10 (1.62-5.92)	70	53.4%	Crude	2.42 (1.28-4.60)	79	60.3%	Crude	2.04 (1.13-3.67)
Control	33	6.8%	Adjusted	1.99 (1.29-3.07)	211	43.7%	Adjusted	2.38 (1.24-4.59)	235	48.7%	Adjusted	2.19 (1.18-4.05)
At or Above in Any One Environment												
Case	53	40.5%	Crude	1.32 (0.87-2.01)	48	36.6%	Crude	1.98 (1.02-3.84)	36	27.5%	Crude	1.45 (0.76-2.75)
Control	191	39.5%	Adjusted	1.44 (0.95-2.19)	177	36.7%	Adjusted	1.81 (0.98-3.33)	151	31.3%	Adjusted	1.47 (0.76-2.84)
All Below												
Case	55	42.0%		1.00	13	9.9%		1.00	16	12.2%		1.00
Control	260	53.7%			95	19.7%			97	20.1%		
Chi-square for trend p-value				0.000				0.008				0.010

Max = Maximum value, RCM = Rate of change metric, TWA = Time weighted average, N = Number of subjects, % = percent.

Adjusted for: Maternal age, interview at gestation, coffee consumption at conception, income, and race.

Table 8. Relative Risk (RR) and 95% Confidence Interval (CI) Assessing the Association of Wire Code, Front Door Magnetic Field Spot and Personal Magnetic Field TWA, RCM, and Max Value for Prospective Sub-study Participants.

	N	% SAB	RR (95% CI)
Wire-Code			
Vhcc	18	0.0	-- (p = 0.58*)
Ohcc	59	8.5	1.3 (0.39-0.42)
Olcc	61	9.8	1.5 (0.48-4.67)
Buried	76	6.6	1.0
Front Door Spot (mG)			
2.0+	14	21.4	3.1 (1.0-9.7)
<2.0	188	8.0	1.0
TWA (mG)			
Bed			
2.0+	20	15.0	2.1 (0.66-6.73)
<2.0	197	7.1	1.0
Home			
2.0+	22	18.2	2.7 (0.97-7.64)
<2.0	195	6.7	
Total Home			
2.0+	20	20.0	3.0 (1.09-8.42)
<2.0	197	6.6	1.0
Other			
2.0+	15	26.7	4.2 (1.54-11.44)
<2.0	189	6.4	1.0
Work			
2.0+	26	0.0	-- (p = 0.13*)
<2.0	122	10.7	
Total 24-hour			
2.0+	22	13.6	1.9 (0.59-6.10)
<2.0	195	7.2	1.0
RCM, Total 24-hr (mG**)			
50th% cutpoint			
0.69 +	108	11.1	2.4 (0.88-6.64)
<0.69	109	4.6	1.0
Max, Total 24-hr (mG)			
50th% cutpoint			
26.85+	109	11.0	2.6 (0.87-7.5)
<26.85	108	4.6	1.0

*Fisher's exact test, 2-tailed.

** Difference between 10 second samples.

Abbreviations: SAB = Miscarriage, TWA=Time Weighted-Average, RCM=Rate of Change Metric, Max=Maximum Value, mG = milligauss, s = second.