Human Adverse Reproductive Outcomes and Electromagnetic Field Exposures: Review of Epidemiologic Studies

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Concerns have been raised regarding a relation between residential and occupational electromagnetic (EM) field exposures and adverse reproductive effects. This paper reviews the epidemiologic evidence for this possible relation, including some pertinent methodologic issues, notes relevant findings from the experimental literature, and discusses areas for future research. Evidence is lacking for a strong association between a woman’s use of a video display terminal (VDT) during pregnancy and spontaneous abortion. The evidence for a strong association between maternal EM field exposures and fetal growth and weight during pregnancy is also lacking, with some suggestive findings for congenital malformations and too few data to reach a conclusion about the magnitude of the effect. With respect to low-level EM field exposures other than VDTs, the paucity of data prevents one from determining whether there are reproductive health risks associated with such exposures. Therefore, this is an area that needs further investigation. Given that altered growth may be an underlying biologic effect of EM field exposures, endpoints that might be pursued in future studies include congenital malformations not associated with chromosomal anomalies, intrauterine growth retardation, and chromosomally normal spontaneous abortions.

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Introduction

In the last 10 years, public concern regarding possible human health effects from exposures to nonionizing electromagnetic (EM) fields has been mounting. Although the primary focus has been on potential carcinogenic effects, there has also been concern that exposures from electric and magnetic fields will result in adverse reproductive effects. This concern is at least partially attributable to numerous reports of clusters of female video display terminal (VDT) users who have experienced spontaneous abortion. Interest has also heightened because of the ubiquity of EM fields and the consequent prevalence of exposure. Clearly, even if risks from exposures are low, the extent of populations exposed in modern society could result in a large disease burden.

Since Wertheimer and Leeper (1) reported the initial observation of an association between electric power lines and childhood cancer, several other investigators have looked for associations between various EM field exposures and childhood cancers (1–6), adult cancers (7–11), and adverse reproductive outcomes (12–36), including congenital malformations, spontaneous abortion, reduced birth weight, and prematurity. A number of reviews (37–41) offer an overview of the epidemiologic literature for EM fields and human health effects. This paper will: a) summarize some of the epidemiologic literature on reproductive endpoints and low-level EM fields, b) note some findings from experimental work possibly relevant to humans, c) discuss some methodologic issues related to epidemiologic research of reproductive outcomes and EM fields, and d) identify areas for future research regarding adverse reproductive outcomes and EM field exposures.

Previous Epidemiologic Research

Studies on reproductive health have investigated a variety of residential and occupational EM field exposure sources including electric blankets, type of home heating, occupations in electrical industries and occupational use of VDTs. For the purposes of summarizing previous epidemiologic findings, studies are grouped into three categories: residential and occupational EM field exposure sources (excluding VDTs) and those examining exposures from VDTs. Potential EM field exposures in these two groups are not mutually exclusive (i.e., VDT use may result in exposures to both extremely low frequency and very low frequency EM fields).

Residential and Occupational EM Field Exposure Studies

Studies that have investigated a possible relation between EM fields and reproductive end points are summarized in Table 1. Wertheimer and Leeper conducted two investigations of residential exposures to EM fields (14,15). The first (14) involved an examination of possible fetal effects from parental use of electric blankets or heated waterbeds. Parents whose baby’s birth was announced in the local newspaper were contacted and interviewed about electric blanket and waterbed use. Data were collected from 1256 index birth families, representing 29% of the total number of births in the study catchment area and time period. Length of gestation was observed to be somewhat longer for infants whose parents used electrically heated beds when those infants were conceived during a season when the need for electric bed heating was greatest. The biologic basis for that observation was not given. This study found no difference between the user and nonuser groups in the proportions of infants weighing less than 2500 g at birth. It did find, however, that among low-weight infants in the user group 46% had gestations of 37 weeks or more, whereas 21% of the low-weight infants in the nonuser group had term gestations. This suggests that parental use of an electrically heated bed may be associated with having a child that is growth retarded. The prevalence of congenital malformations was too low to evaluate among the 528 siblings. Abortions (induced or spontaneous) occurring in the one year preceding conception of a live birth (index birth or sibling) were more common among
**Table 1. Studies of electric and magnetic field exposures**

| Reference             | Study design  | Subjects included in study                          | Study outcome definition                          | Source of outcome information                        | Study period               |
|-----------------------|---------------|-----------------------------------------------------|---------------------------------------------------|------------------------------------------------------|---------------------------|
| **Residential exposures** |               |                                                     |                                                   |                                                      |                           |
| Wertheimer and Leeper (14) | Cohort       | 1256 Denver births 692 earlier siblings            | Birthweight, previous abortions, gestational length | Birth announcements, earlier birth certificates, questionnaire | 1982 for index births 1975–1981 for previous pregnancies |
| Wertheimer and Leeper (15) | Cohort       | 1879 Oregon liveborns with traceable addresses of and information on type of home heating | Fetal losses < 20 weeks gestation 1 year prior to conception of live birth | Birth certificates                                              | 1983, 1985                |
| Dlugosz et al. (16)   | Matched case-control  | 542 cases, 542 controls, New York                  | Neural tube and oral cleft defects                | New York Malformation Registry                          | 1983–1986                |
| Eckert (34)           | Case study    | 294 infants who died from Sudden Infant Death Syndrome, Germany | Sudden Infant Death Syndrome                      | ?                                                      | 1961–1967                |
| **Occupational exposures** |               |                                                     |                                                   |                                                      |                           |
| Knave et al. (12)     | Cross-sectional | 53 workers in high voltage jobs in Sweden, 53 workers in low voltage job | Fertility measured by number of children and sex ratio | Questionnaire                                              | 1952–1975                |
| Nordstrom et al. (13) | Historical cohort | 880 pregnancies among 372 male workers' spouses in Sweden power occupations | Birthweight, perinatal death, spontaneous abortions, and congenital malformations | Mail survey and medical records verification              | 1953–1979                |
| Buiatti et al. (17)   | Case-control  | 112 infertile males and 127 male controls with normal sperm counts, Italy | Male infertility                                  | Single hospital/clinic population                       | 1979–1981                |
| Hemminki et al. (18)  | Historical cohort | 195 spontaneous abortions among 35,000 female members of Union of Metal Workers, Finland | Spontaneous abortion                              | Hospital discharge registry                               | 1973–1976                |
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(residential and occupational) and adverse reproductive outcomes.

| Exposure definition                                      | Source of exposure information | Timing of exposure | Maternal or paternal exposure | Results |
|----------------------------------------------------------|--------------------------------|--------------------|-----------------------------|---------|
| Use of an electric blanket or heated previous 8 years    | Telephone interview           | Selected periods around pregnancy during | Maternal and paternal | No difference noted for low birthweight, some evidence for intrauterine growth retardation among exposed births, abortions higher in previous pregnancies among exposed, and abortions followed a seasonal pattern of need for blanket use |
| Home with ceiling cable heat                             | Assessor’s office files        | Time of fetal loss | Assumed maternal            | Abortion frequency not higher in homes with ceiling cable heat. A positive correlation was found between the fetal loss ratio for ceiling cable heated homes and the increase in heating degree days |
| Use of electric blankets and waterbeds by setting and season | Mail survey                    | First trimester   | Maternal                    | Risks for neural tube defects (odds ratio = 0.9), cleft lip +/- palate (odds ratio = 0.7), and cleft palate (odds ratio = 0.8) not increased for electric blanket users vs. nonusers, results similar for waterbed use |
| Floor level of residence                                 | Address books                  | Time of infant death | ?                         | Larger number of cases lived on basement or first floors than on higher floors |
| Employment in high-voltage job for more than 5 years     | Employment records            | Before child’s birth | Paternal                   | Fewer children born to exposed fathers but difference present before “exposed” workers had started high voltage jobs; fewer boys among exposed fathers |
| Occupation groups: high-voltage switchyard workers (400 kV), construction workers in switchyard (130-200 kV), other electric field exposure (<70 kV) | Employment records            | Conception         | Paternal                   | Smaller proportion of male births among switchyard workers, 3-fold higher prevalence of congenital malformations in switchyard offspring, switchyard workers reported more difficulty fathering children no other endpoint elevated among exposed |
| Occupation in the radioelectric industry                | Face-to-face interview         | Longest held occupation | Paternal                   | Increased risk observed for men employed in radioelectric industry; odds ratio = 5.9, 95% confidence interval (0.86, 40.2) |
| Occupations in electronic branch of metal industry       | Union records                  | While member of union | Maternal                   | Age-standardized rate of spontaneous abortions for electronics workers was 8.0% and for radio and television workers 12.0% compared with 5.5% and 4.8% before becoming a member |
electric blanket users (7.8%) and waterbed users (6.3%) than among nonusers (4.2%). An uneven seasonal distribution of abortions was observed among electric blanket users, with all 24 occurring between September and June. This uneven distribution was not observed among waterbed users or among nonusers.

While this study suggests an association between electric bed-heating devices and fetal growth or fetal loss, the following methodologic considerations may have influenced results in a direction that is difficult to predict: the method for identifying subjects (i.e., published birth announcements), the source of reproductive end-point and covariate information (i.e., birth certificates), the nonindependence between index births and their siblings, and the exclusion of fetal losses among primigravid women. In addition, as the authors note, results do not differentiate whether the associations might be related to the thermal effect of the bed heating devices or to the EM field produced by the bed heaters.

In an effort to disentangle thermal versus EM field effects, Wertheimer and Leeper (15) investigated whether homes with ceiling cable heat (EM fields are higher from this heating source than from baseboard heating) were associated with increased fetal losses compared to homes with other types of heating sources. The investigators selected a sample of Oregon births from 1983 and 1985 and identified prior fetal losses (less than 20 weeks gestation) among their mothers, as reported on the birth certificate of the index birth. They compared the ratio of fetal losses in cable heat homes to the ratio in homes with other types of heating and did not find a difference (0.076 versus 0.075). (The number of previous fetal losses was the numerator, but the denominator did not include the number of births from the same cohort of conceptions as the fetal losses; rather, it was the number of index births.) A positive correlation was observed between a monthly ratio of fetal loss at ceiling cable heat homes (relative to homes without cable heat) and the increase in heating degree days reported for that month.

These data, along with their previous observations from Colorado, were interpreted by the investigators as evidence that the number of fetal losses (not computed as a rate) was elevated in months when cold weather was increasing, a time period they argued was also associated with increasing EM field exposures resulting from increased use of ceiling cable heat. As in their previous study, history of pregnancy loss was obtained from a cohort of women who had a more recent pregnancy resulting in a live birth. Thus, fetal losses among primiparous women were not eligible for this study. Data on possible confounders, such as infections or possible risk factors that might follow similar seasonal distributions (but also would have to be related to homes with ceiling cable heat), were not available. Nevertheless, these observations are suggestive and need follow-up by more rigorous study methods.

The only study done to date that has investigated a possible relation between congenital malformations and residential exposures to extremely low frequency EM fields was performed by Dlugosz et al. (16). However, details of this investigation have not yet been published so that a critical assessment of the study’s null results is premature.

Another study of residential exposures to EM fields concerned sudden infant death syndrome (34). Although the sudden death of an infant is a postnatal event, the possibility of death resulting from a prenatal event may warrant consideration of this condition as an adverse reproductive outcome (42). The investigator observed that among 294 infants who died of sudden infant death syndrome in Hamburg, Germany, more had lived in basement or first floors, and he argued for an association between EM fields and sudden infant death based on the assumption that lower floors are more likely to have “uncommon magnetic fields or stray electric currents in the ground.” The crude exposure definition and the comparisons of number of infant deaths by floors without an estimate of the population at risk make the interpretation of this study difficult.

The earliest epidemiologic study of reproductive health effects from occupational exposures to EM fields was conducted by Knave et al. (12). They sought to identify whether fertility (and other chronic health effects) was compromised among men working in high-voltage (50 Hz and 400 kV) substations in Sweden for more than 5 years compared to men having occupations with low-voltage EM fields. Results showed that men exposed to high-voltage EM fields had fewer children than men working in low-voltage occupations. This difference, however, was seen prior to the date the exposed men began work in a job that involved high-voltage EM fields. The difference in number of children might have indicated that the men working in high-voltage conditions, as a group, were less frequently attempting to have children. The investigators also observed an altered sex ratio, with a paucity of male children, and concluded that work in high-voltage substations could not be ruled out as a possible explanation for this result. This nonspecific result may be suggestive of reproductive damage associated with occupations in areas having high-voltage EM fields.

Nordstrom et al. (13) also studied men working in high-voltage areas for increased frequencies of spontaneous abortions, perinatal death, congenital malformations, altered sex ratio, and reported fertility problems. A cohort of 542 male employees of Swedish power facilities completed a questionnaire about employment characteristics, pregnancy and fertility problems (spontaneous abortions verified in medical records), and possible confounders. Pregnancies among spouses of male switchyard workers in 400-kV substations were considered exposed. Pregnancies among spouses of males not employed as switchyard workers, but employed with the power facilities, were considered the reference group. Some pregnancies among the spouses of switchyard workers were also considered in this group for the periods the male workers were not employed in the switchyard. The prevalence of congenital malformations among children of switchyard workers was three times that of the reference group. The malformations among these infants reflected a heterogeneous group of diagnoses. Switchyard workers were about twice as likely to report fertility problems and had somewhat fewer male offspring compared to reference workers. The latter finding is consistent with the altered sex ratio noted by Knave et al. (12). Spontaneous abortions were not more common among switchyard workers. Results were not influenced by adjustment for parental cigarette smoking, alcohol use, medication use, maternal age, or a variety of other possible confounders. These data, although too sparse for analyses of specific end points such as detailed malformation groupings, are suggestive of an association with males’ preconceptional exposures and subsequent malformed offspring. Because the separation of groups with differing exposure levels may have been incomplete, a true association could have been underestimated in this study.

In a case–control study of 112 infertile males (azoospermic or oligospermic) and 127 males with normal sperm counts, Buiatti et al. (17) found an odds ratio of 5.9 associated with employment in the radioelectric industry. The elevated risk was imprecise (95% confidence interval = 0.86, 40.2), and no details were provided about the possible electric and magnetic field exposures that might be associated with occupations in the radioelectric industry.

Hemmi and colleagues (18) observed an increased rate of spontaneous abortion (spontaneous abortions/births + induced abortions + spontaneous abortions) for electronics workers among a cohort of 35,000 female Finnish members of the Union of Metal Workers. The increase was primarily among women involved with the production of radios and televisions. The age-standardized rate among radio and television workers was 12%, compared with 4.8% in the same women before joining the Union.
Within the subgroup of radio and television production workers, the investigators noted an excess of spontaneous abortions among women who were exposed to solder. Finding an increase of spontaneous abortions among electronics workers may be interesting in light of increased risks for women employed in the semiconductor industry found by others (43), but it does not specifically implicate EM field exposures.

Video Display Terminal Use Studies

Many studies have researched reproductive effects related to VDT use during pregnancy and have focused primarily on potential risks for spontaneous abortions (19,20,22–28,35,36) and congenital malformations (23,24,26,27,29–33) and given less attention to other specific adverse reproductive outcomes (20,21,26–28,32,33). The technical aspects associated with the use of VDTs along with a discussion of possible health implications of working with a VDT have been reviewed by Bergqvist (44). Further, others (45,46) have reviewed much of the epidemiologic research regarding VDT exposures, and a detailed summary of the studies done to date is provided in Table 2. Because the recent study by Schnoor et al. (25) has not been reviewed elsewhere, details of this study are summarized below.

Schnoor et al. (25) compared the prevalence of spontaneous abortions in a cohort of female telephone operators who used VDTs at work to a cohort of female telephone operators who did not use VDTs at work. These two cohorts had similar work situations with the exception of VDT use; therefore, some control for physical and psychologic stress was obtained. A total of 730 married women between the ages of 18 and 33 who had pregnancies during the study time period participated in the study. Among the 323 VDT users, 14.8% of the pregnancies ended in spontaneous abortion, compared to 15.9% among the 407 who did not use a VDT. The percentage of spontaneous abortions was also similar between nonusers and users of 1 to 25 hours per week (15.6% versus 17.2%) and >25 hours per week (15.6 versus 15.4%). Analyses involving potential confounders, early versus late abortions, and only physician-verified abortions did not alter the findings. A sample of the work environments in this study were subjected to measurements of electric and magnetic fields. The VDT users were exposed to levels of extremely low-frequency emissions in the range of exposures similar to exposures in the home and for comparison operators. Unlike others, this study provided some control for psychosocial stress and ergonomic factors and some measurement data on EM field emissions from VDTs. However, it did not have the power to rule out the weak association (approximately a 20% increased risk) observed in earlier investigations.

Findings from Experimental Work

Studies using various animal models have been conducted to investigate potential biologic effects resulting from exposures to electric and magnetic fields, and conflicting evidence regarding the ability of these fields to influence prenatal development has emerged. Juutilainen (47) has recently summarized the effects of low-level fields on embryonic development. While some studies, mainly of chick embryos, have reported developmental effects (48–62), several other studies found no effects (63–69). In studies where effects have been reported, the observed developmental deficits include various congenital anomalies, developmental delay, altered sex ratio, fetal loss, reduced fertility, and demasculinization. The mechanisms underlying these developmental abnormalities are unknown (70). These studies have included a variety of exposure paradigms, such as different waveforms, field intensities, exposure durations, and field types (electric, magnetic, or both). The effect of the earth’s magnetic field has not always been considered, yet has been shown to influence results in some studies (71). Dose–response relations have generally not been observed. Rather, effect windows have been noted in some studies where animal embryonic models subjected to particular field strengths exhibited aberrant development, while animals exposed to field strengths above or below did not (48,57).

Studies with cellular test systems have shown that electric and magnetic fields at specific frequencies and intensities are capable of resulting in biologic effects (72,73). Although the exact mechanisms for these interactions are unknown, one theory suggests that cells have their own weak electrical signals that enable them to “whisper together,” which allows for cell-to-cell communication for normal health (73). Disrupted communication by exposure to EM fields may result in unregulated growth (73). Evidence from other studies suggests that electric and magnetic fields may alter growth (74,75), enhance DNA synthesis (76), and influence the modulation of calcium binding to cell surface molecules (77). Growth, DNA synthesis, and calcium binding are relevant mechanistically to normal embryogenesis, and alterations to these processes by EM fields suggest that exposure to these fields could result in adverse reproductive effects.

Conclusions that may be drawn from the experimental studies are limited by the inconsistent findings resulting from differences in study design, animal model, and exposure paradigm considered. Many of the positive associations observed among animal models have not been replicated across laboratories, and effects observed from in vitro studies have been less evident or not present in in vivo systems (78), which suggests that the developing fetus may be protected by physical or physiologic maternal attributes. It is clear that exposure to various aspects of EM fields can produce biologic effects in experimental systems; however, the interpretation of these effects in terms of risks to human reproduction needs substantial clarification.

Methodologic Issues

Previous epidemiologic research in this area can be interpreted in the methodologic contexts of: a) issues with study endpoints, b) issues with exposure assessment, and c) other design and analytic considerations. The emphasis of discussion here is on the more common end points studied (i.e., spontaneous abortions and congenital malformations).

Study End Point Issues

The decision to investigate a particular reproductive health effect in relation to a putative exposure is generally based upon the biologic plausibility of such an association as suggested by previous epidemiologic or teratologic data, anecdotal reports made by astute clinical observers, or reports of disease clusters. Based on the concern derived from reports of seemingly unusual aggregations of spontaneous abortions and congenital malformations occurring among VDT users (44), and on the observed association between childhood cancer and residential exposure to EM fields (1,3,4,6), a variety of reproductive health effects from both residential and occupational EM field exposures have been investigated (Tables 1, 2).

An issue relevant to some of the end points studied is the specificity with which they have been defined for analysis. For example, among the studies that investigated congenital malformations in relation to various EM field exposures (Tables 1, 2), many considered all malformations as a single analytic group. Based on observations with known teratogens, exposures are unlikely to result in a general increase in all types of malformations, although, depending on the timing of exposure, they may increase the risk of more than one type. However, based on the nonspecific biologic effects observed in experimental work of EM exposures, it is not clear how one might better define malformation groups for analysis. Studies of spontaneous abortions might also be criticized for heterogeneous endpoint definitions. Although a few studies (20,25) have analyzed early and late spontaneous abortions separately, no study has included karyotype information on aborted fetuses. Spontaneous abortions are etiologically heterogeneous, with approximately 30% to 50% being chromosomally...
| Reference                  | Study design     | Study outcome definition                                                                 | Source of outcome information            | Study period | Subjects included in study                                                                 |
|----------------------------|------------------|------------------------------------------------------------------------------------------|------------------------------------------|--------------|------------------------------------------------------------------------------------------|
| Lewis et al. (35)          | Case–control     | Spontaneous abortions (< 20 weeks)                                                       | Questionnaire (self-administered)        | 1980–1978    | 30 South Australian spontaneous abortion cases and 60 controls matched on maternal age and on delivery date |
| McDonald et al. (24)       | Historical cohort| Clinically recognized spontaneous abortions, congenital malformations                     | Medical records, maternal interview      | 1982–1984    | 9471 pregnancies from among 56,012 women in Montreal; also 8161 previous pregnancies from same women |
| Kurppa et al. (29,31)      | Case–control     | Malformations of central nervous system, cardiovascular system, skeleton or oral clefts  | Finnish Register of Congenital Malformations | 1976–1982    | 1475 Finnish infants with malformations; 1475 paired referents |
| Ericson and Kallen (26)    | Historical cohort| Stillbirth, neonatal death, birthweight <2500 g, malformations, clinically recognized spontaneous abortions | Swedish Registries                       | 1976–1977    | 10,025 Swedish women working in selected white collar occupations |
| Ericson and Kallen (27)    | Case–control     | Stillbirth, neonatal death birthweight <1500 g, malformations, clinically recognized spontaneous abortions | Swedish Registries                       | 1980–1981    | 429 cases and 926 controls of similar maternal age who worked outside home in Sweden |
| Westerholm and Ericson (36)| Historical cohort| Hospitalized spontaneous abortion rate, malformations, birthweight, perinatal mortality, stillbirth | Swedish Registries                       | 1980–1983    | 4117 pregnancies among female clerks at social security bureaus in Sweden |
| Butler and Brix (28)       | Historical cohort| Stillbirth, spontaneous abortions                                                         | Questionnaire, medical records           | 1980–1985    | 817 pregnancies among 728 female clerical workers in Michigan |
| Goldhaber et al. (23)      | Case–control     | Spontaneous abortions, malformations                                                       | Medical records, birth certificates       | 1981–1982    | 452 cases and 723 liveborn controls |
| Nurminen and Kurppa (21)   | Historical cohort| Threatened abortion, length of gestation, birthweight, placental weight, and maternal blood pressure | Medical records, questionnaire           | 1976–1982    | Finnish women, referents from earlier malformation study, 60 VDT working mothers, 179 non-VDT working mothers |
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and adverse reproductive outcomes.

| Exposure definition                      | Source of exposure information | Timing of exposure | Maternal or paternal exposure | Results                                                                 |
|-----------------------------------------|--------------------------------|--------------------|-------------------------------|--------------------------------------------------------------------------|
| Average number of hr/wk using VDT at work | Questionnaire                  | During pregnancy   | Maternal                      | Odds ratio for any VDT use was 1.7 for all spontaneous abortions          |
| Number of hr/wk using VDT at work       | Questionnaire                  | When worker first suspected she was pregnant | Maternal                      | Spontaneous abortions among current pregnancies: observed/expected for nonusers was 0.89, for users 1 to 6 hr/wk 1.24, for users 7 to 29 hr/wk 1.25, for 30+ hr/wk 1.12. Malformations: among current pregnancies prevalence was 3.3% in VDT users vs. 3.7% in nonusers. Among previous pregnancies the prevalences were 3.8% vs. 3.6%. |
| VDT use determined by industrial hygienist, based on occupational title grouped as 1 to 4 hr use/day or 4+ hr use/day | Questionnaire                  | First trimester    | Maternal                      | Odds ratios for any VDT use were 0.4 for central nervous system, 0.9 for oral clefts, 0.8 for skeletal defects, and 1.8 for cardiovascular defects |
| Occupational groups assumed to have high, medium, low potential for VDT use | Census data                    | One or two years prior to delivery | Maternal                      | Higher frequency of infants born weighing <1500 g or <2500 g among women in medium exposure group; no excesses noted for malformations, spontaneous abortions, or neonatal deaths |
| Number of hr/wk using VDT at work       | Mail survey                    | Selected periods during pregnancy | Maternal                      | Odds ratios for VDT use 20+ hr/wk = 2.3 for birth defects, 1.2 for spontaneous abortions and for any VDT use, 1.6 for birth defects and 1.1 for spontaneous abortions |
| VDT use at work classified into 5 exposure groups based on frequency of use | Trade union and employment records | During 1980–1983 | Maternal                      | No deviance from expected for stillbirths, perinatal mortality, spontaneous abortions or birthweight; a 2-fold excess was observed for significant malformations among exposed <10 hr/wk |
| Number of hr/wk using VDT at work       | Questionnaire, employment records | During pregnancy   | Maternal                      | Stillbirths and spontaneous abortions 1.2 times higher than expected among users of VDTs >20 hr/wk |
| Number of hr/wk using VDT at work       | Mail/telephone questionnaire    | First trimester    | Maternal                      | Odds ratios for VDT use 20+ hr/wk = 1.8 for spontaneous abortion, 1.4 for birth defects, and for any VDT use, 1.2 for spontaneous abortions, and 1.2 for birth defects |
| VDT use determined by industrial hygienist based on occupational title grouped as 1 to 4 hr use/day or 4+ hr use/day | Questionnaire                  | First trimester    | Maternal                      | No difference noted between VDT workers and non-VDT workers |

(Continued)
abnormal (79). One would expect that if exposures to EM fields increase the risk for spontaneous abortions then the timing of exposures would be different for early and late spontaneous abortions. The inability to form etiologically homogeneous endpoint groups for analysis may result in an attenuated measure of a true effect.

Another issue of general concern regards the source of endpoint information. Studies have used a variety of sources, including vital records, parental interviews, medical records, pathology records, and malformation registries (Tables 1, 2), to ascertain reproductive health effects. The use of different sources probably results in different prevalence estimates for a given adverse reproductive outcome. A woman’s report of a spontaneous abortion, her child’s birthweight, or congenital malformation has been shown to be susceptible to error when compared to hospital records (80,81). This finding would also suggest that birth certificate data on prior pregnancy loss, as reported by mothers, would also be suspect. At least two studies relied on such information (14,15).

Further, the studies done to date have ascertained clinically recognized spontaneous abortions. However, many pregnancy losses occur prior to the recognition of pregnancy (82). Interestingly, at least one study (20) of spontaneous abortions from VDT use found a higher risk for early (<13 weeks gestation) spontaneous abortions than for late abortions. Even among recognized spontaneous abortions, the timing of diagnosis during pregnancy has varied in these studies [e.g., < 20 weeks (20) or < 28 weeks (25)]. The opportunity for bias is present if a subject’s exposure is related to when her pregnancy is recognized. The earlier a pregnancy is recognized the greater the likelihood is that an early spontaneous abortion will be recognized. Goldhaber et al. (23) noted that pregnancies among VDT users were diagnosed an average 4 days earlier than nonusers, and they therefore controlled for this difference analytically. Cultural, ethnic, or educational variations might result in

| Reference | Study design | Subjects included in study | Study outcome definition | Source of outcome information | Study period |
|-----------|--------------|---------------------------|--------------------------|-------------------------------|--------------|
| Bryant and Love (22) | Case–control | 334 spontaneous abortion cases, 334 prenatal controls, and 334 postnatal controls in Canada | Spontaneous abortions where women required hospitalization | Medical records | 1984–1985 |
| Nielson and Brandt (19) | Case–base | 666 spontaneous abortion cases and 764 pregnancies in referent group from clerical and commercial workers in Denmark | Clinically recognized spontaneous abortions | Medical registers | 1983–1985 |
| Brandt and Nielson (30) | Case–base | 421 congenital malformations and 1365 pregnancies in referent group from Denmark | Malformations | Medical registers | 1983–1985 |
| Tikkanen et al. (32) | Case–control | 500 infants with cardiovascular malformations; 1055 nonmalformed infants from Finland | Cardiovascular malformations, length of gestation, weight, placental weight | Finland malformation registry and children’s cardiac registry | 1982–1984 |
| Bjerkedal and Egenaes (33) | Historical cohort | 1820 pregnancies among female postal employees in Norway | Malformations, stillbirth, early neonatal death, perinatal death, birthweight, perinatal death, birthweight, placental weight | Norway malformation registry, medical birth registry | 1967–1984 |
| Windham et al. (20) | Case–control | 439 spontaneous abortion cases, 909 live-born controls in a California county | Spontaneous abortion (≤20 weeks), low birthweight, intrauterine growth retardation | Pathology labs | 1986–1987 |
| Schnorr et al. (25) | Cohort | 323 VDT using operators and 407 non-VDT using operators in U.S. | Spontaneous abortion (≤28 weeks) | Questionnaire, vital records | 1983–1986 |
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| Exposure definition | Source of exposure information | Timing of exposure | Maternal or paternal exposure | Results |
|---------------------|--------------------------------|-------------------|------------------------------|---------|
| Number of hr/wk using VDT at home or work | Questionnaire | Period between 3 months prior and 4 months post-LMP | Maternal | Odds ratio for any VDT use was 0.81 using prenatal controls and 1.1 using postnatal controls; odds ratio for >21 hr/wk use was 1.1 using either prenatal or postnatal controls |
| Number of hr/wk using VDT at work | Questionnaire | During pregnancy | Maternal | Odds ratio for any VDT use was 0.92, and 0.76 for >30 hr/wk compared to no VDT use |
| Number of hr/wk using VDT at work | Questionnaire | During pregnancy | Maternal | Odds ratio for any VDT use was 0.96, and 1.0 for >30 hr/wk compared to no VDT use |
| VDT use determined by industrial hygienist, based on occupational title grouped as 1 to 4 hr use/day or 4+ hr use/day | Questionnaire | First trimester | Maternal | Odds ratio for any VDT use was 1.2 and for 20+ hr/wk was 1.4 compared to no VDT use for cardiovascular malformations; no relation between VDT use and fetal growth indicators |
| Time period when VDTs present in work place 1979–1984 | Employment records | Employed at end of of pregnancy | Maternal | Perinatal mortality 1.7% vs. 0.8%, low birth weight 1.1% vs. 0.8%, prematurity 9.0% vs. 6.5%, congenital malformations 6.2% vs. 5.2% among exposed vs. before period or after employment |
| VDT use at work defined as number of hr/wk and number of weeks during pregnancy | Questionnaire | During pregnancy | Maternal | Odds ratios for all abortions: <20 hr/wk = 1.2, ≥20 hr/wk = odds ratio for early (<13wk) abortions: <20 hr/wk = 1.5, ≥20 hr/wk = 1.4 |
| Hr/wk and weeks during first trimester employed as a directory-assistance operator | Employment records | First 28 weeks of pregnancy | Maternal | Percent of spontaneous abortions were 14.8% vs. 15.9% for VDT users vs. nonusers; 17.2 vs. 15.6% for 1-25 hr/wk use and 15.4 vs. 15.6% for 25+ hr/wk use among users versus nonusers |

Differences of when a pregnancy is diagnosed, and therefore result in differences in the observed number of clinically recognized spontaneous abortions (45,83). If such variations are related to a woman’s exposure, the opportunity for biased effect estimates may exist.

**Exposure Assessment Issues**

Differences in biologic effects are associated with various frequencies in the EM spectrum (84). Power frequency fields (50–60 Hz), in contrast to ionizing radiations like X rays, are incapable of breaking chemical bonds, and in contrast to microwaves, do not cause tissue heating (84). Also noteworthy is that some physical and biologic properties of electric and magnetic fields are distinct. Methodologic issues relevant to studies concerning exposure pertain to the definition of exposure: what it is; to whom (mother, father, or fetus) and when in the peri-conceptional period it occurs; the amount (dose) experienced by a study subject; how it is measured; from where information about it was obtained. Definitions of exposure (Tables 1, 2) have involved seemingly heterogeneous exposures, such as working in a 400-kv switchyard (13) and home use of an electric blanket (14,16). Studies have differed in both the frequency range studied and the type of field (electric or magnetic) investigated. Those examining risks from VDT use were primarily interested in very low frequency EM fields, and investigations of electrically heated bed-warmer focused on exposure to extremely low-frequency fields. In the occupational studies of electrical workers (2,12,13,17,18), it is not clear whether risks from electrical fields or magnetic fields were being assessed. In addition, higher frequency field exposures have been examined by other investigators (85–90). Even though there is a general lack of information regarding the biologic effects on reproduction from certain areas of the EM spectrum, a discussion of these exposures and studies is beyond the scope of this review.

Aspects surrounding when and to whom an exposure occurred are also important to
consider. A general principle of teratogenesis is that the ability of an exposure to result in an adverse effect is conditional on the timing of that exposure relative to the developing fetus (90). Failure to specifically obtain exposure information for a critical time period may produce a risk estimate biased toward the null value. EM field exposures to a man or woman prior to conception may be relevant to reproductive health effects, such as subfertility or germ cell damage, but may not be relevant to chromosomal damage in the conceptus, given that EM field exposures have not been shown to be mutagenic (91). In general, various types of exposures (e.g., medications) a mother encounters during specific periods of pregnancy are plausible risk factors for congenital malformations (92), spontaneous abortions (79), reduced birth weight (93), and certain childhood cancers (94). However, there is less support for the notion that various exposures the father or mother receives prior to conception or the father receives during pregnancy may act as risk factors for these outcomes. Studies on risks of VDTs (Table 2) were exclusively interested in maternal use and predominantly for exposure during early pregnancy [but not exclusively (19,30,35)], whereas studies involving other EM field exposures (Table 1) involved both maternal and paternal exposures for several periconceptional time periods.

Another relevant issue concerns the extent or dose of exposure. There are multiple sources of low-level EM fields in our environment (84), resulting in some level of exposure to most individuals. With the exception of the study by Bryant and Love (22), who sought information on both home and work exposures to VDTs, no study considered other sources of possible exposures to EM fields beyond the single exposure of interest. The implication of neglecting these other sources is that variations in EM field exposure among individuals in the study populations might be overlooked. Such misclassification errors probably would reduce the magnitude of estimated effects (95). It is unclear, however, what the etiologically relevant measure of exposure is (e.g., time-weighted average, peak frequency, or some other parameter of exposure). Some experimental work (48) implies that certain biologic effects are not monotonically related to dose but depend on windows in the exposure range. In terms of measuring exposures, only one study (25) incorporated direct field exposure measures. Most studies have relied on self-reported surrogate exposures (e.g., number of hours per week using a VDT) (19,20,22–24,27,30), occupation in electronics industry (17), or residence in cable heat homes (15).

Potential errors in assessing exposure in these studies may be associated with the source of exposure information. Exposure information (Tables 1, 2) was derived primarily from self-reported questionnaire data, employment records, and other existing data sources. Querying study subjects allows for collection of detailed data on characteristics of possible field exposures, such as source and timing. However, this approach may be susceptible to information bias (96), as suggested by some investigators (24,27). Although studies concerning reproductive outcomes are often criticized on the basis that the group with the endpoint under study will remember past events better than those in the referent group, studies that have tested specifically for recall bias have been unable to demonstrate its presence (97–99). However, potential for recall bias may increase as public concern about EM field exposures heightens. Studies that used employment records to obtain exposure information are not subject to problems with recall, but information on an individual’s work habits that may be relevant to EM field exposures may not be available. Similarly, the assignment of exposure status by an industrial hygienist (21,26,29,31,32) based on occupational title or group information may not account adequately for individual variations in exposure within an occupational classification. Either limitation might result in misclassification of exposure status and a resultant dilution of measured effect estimates (95).

Other Design and Analytic Issues

Because all humans are exposed to electric and magnetic fields to some extent, the selection of a completely unexposed reference population is impossible. If a sizable proportion of the reference population is also exposed, ability to uncover risks associated with those exposures may be diminished. However, if information on multiple sources of exposure is available for both the case and referent populations, estimation of risks from selected exposures will be enhanced.

An examination of possible confounders in studies of risks from EM fields, although important, may be problematic for two reasons. First, because there is a lack of information on what the exposure is, it is difficult to identify other factors that are related to the exposure and increase the risk for the reproductive outcome of interest. A second problem is that, in general, there are not many established risk factors for adverse reproductive outcomes other than lower birth weight.

Sample size is often a problem in studies of specific reproductive endpoints. Because some reproductive endpoints are rare, the practice of broadly grouping endpoints is often undertaken. However, this is of dubious biologic validity. This issue is of particular concern for some of the studies that investigated congenital malformations (13,24), but it also may be relevant to studies of spontaneous abortions that do not include karyotype information. Teratogenic agents appear to increase the risk for specific malformations. One would not expect that all types of malformations would be increased from low-level EM field exposures during pregnancy, nor would one expect to see all types of spontaneous abortions (i.e., early versus late or chromosomally normal versus abnormal) increased. The determination of sample size requires consideration of these biologic issues.

Future Research

Concerns regarding the potential for residential or occupational EM field exposures to result in adverse reproductive effects have been raised. Overall, epidemiologic evidence is lacking for a strong association between a woman’s VDT use during pregnancy and for that pregnancy to end in spontaneous abortion. The relations noted thus far have, with the exception of Goldhaber et al. (23), shown about a 20% increased risk for VDT users. If this small increase reflects causality and is not due to uncontrolled confounding or to artifact, it would be important from a public health perspective, given the large number of women who use VDTs during pregnancy. Evidence for increased risks for other adverse reproductive end points from VDT use is equivocal. Some suggestive findings for malformations will require follow-up. Even increased risks for early spontaneous abortions (20), which may be indicative of a teratogenic effect if the frequency of malformed fetuses is greater among these earlier abortions than among later abortions (100), will need follow-up. Too few data exist to reach a conclusion about other reproductive health effects from VDT use.

To elucidate the potential relationship between VDT use and spontaneous abortion risk, further investigations will require large numbers of study subjects, improved measures of exposure (e.g., direct measurement of field emissions from VDTs, distance from VDT, proximity to other sources of EM fields, orientation of worker to VDT), consideration of the heterogeneous nature of the end point studied (i.e., chromosomal versus nonchromosomal), inclusion of early as well as late spontaneous abortions, and consideration of the competing hypotheses related to physical and psychosocial stress (101,102).
Monson (103) has suggested that future investigations of reproductive risks in relation to VDT use will need to be prospective in their design. Although common adverse reproductive effects such as spontaneous abortion or reduced birth weight may be amenable to a prospective design, the rarity of specific malformations (e.g., prevalences at birth of 1 per 1000 for common malformations), argues against the prospective approach based on pragmatic and economic considerations. Unless large occupational cohorts are available, prospective studies of malformation risk resulting from maternal VDT use would be hard to justify.

Clearly, the heightened public awareness about possible reproductive risks from VDT use may introduce difficulty in obtaining accurate exposure information from retrospective studies. Therefore, retrospective studies involving reproductive end points, such as congenital malformations, will need to be creative in validating exposure information. For example, in addition to collecting detailed information from a parent about VDT use, studies might attempt to acquire information from employers about a parent's work schedule and conditions surrounding VDT use. Other reproductive end points like low birth-weight and intrauterine growth retardation may be studied economically by using reference groups from retrospective investigations of malformations and spontaneous abortions, as some investigators have done (20,21,32).

The epidemiologic evidence regarding the potential reproductive risks from exposure to low-level EM fields other than VDTs is even more lacking (Table 1). These studies reflect a variety of endpoints and field exposure sources, yet taken as a whole, they do not suggest strong associations between adverse reproductive effects and EM field exposure. However, it seems prudent to resist drawing conclusions about the potential reproductive risks from low-level field exposures until additional investigations are performed.

To date, only three studies have investigated residential exposure to EM fields and adverse reproductive effects: two explored exposures from electric bedwarmers and specific congenital malformations (16) and fetal loss (14), and one examined pregnancy loss and power-frequency field exposures from home heating (15). All three studies focused only on maternal exposures. In contrast, most occupational studies have investigated paternal exposure to EM fields.

There is a need for investigations of other sources of residential EM field exposures (e.g., transmission and distribution lines, electric appliances and power tools, or electric train lines). In addition, future research needs to incorporate additional methods, such as personal monitors or spot measurements or wiring codes, for assessing the exposure (or its surrogate) that appears to be related to childhood cancers (1,3). Retrospective studies could provide much needed descriptive data (primarily from the referent group) on the prevalence of exposures from these and other sources. Without this information, the choice of exposed groups to follow in prospective studies of adverse reproductive effects would be difficult to make.

Although there is little support for paternally mediated adverse reproductive effects (104), some studies have suggested altered sex ratios among the offspring of exposed fathers (12,13), and at least one study has suggested an association between paternal EM field exposures and childhood cancers in offspring (2). Thus, paternal residential exposure to EM fields, from a variety of sources and preconceptional time periods, may be an avenue worthy of additional investigation.

Future occupational studies might focus on maternal exposures to EM fields. Job exposure matrices, as used for studies of other occupational exposures and disease endpoints, would be useful to develop. However, to avoid errors associated with exposure misclassification, a sizable amount of exposure-based research would first have to be completed to ensure that occupations were accurately classified with respect to EM field exposures.

No study has considered any adverse reproductive health effect from combined home and work exposures to low-level fields. Schnorr et al. (25) reported that VDT users had abdominal measurements in the range of exposures that would be experienced at home, but no study has attempted to estimate a person's total exposure to low-level fields. Certainly, studies that have not found associations between EM field exposures and adverse reproductive effects may have failed to do so because total exposures were not considered.

Given what little is known about the attributes of the exposures being estimated, it seems unlikely that more descriptive types of epidemiologic study designs employing existing data sources will be very revealing. For example, studying seasonal variations for reproductive endpoints based on the assumptions about risk used by others (14,15) is simple if existing data sources can be utilized, but the interpretation is quite difficult given the nonspecificity of the analysis and the underlying assumptions about seasonal variation in risk.

The experimental work thus far offers little direction to epidemiologists interested in reproductive health effects, except it shows that numerous aspects about exposures appear to be relevant (e.g., waveform, frequency) and that growth may be altered by EM fields. Altered growth may be mechanistically important to many adverse reproductive endpoints, but it is nonspecific. Given that EM field exposures do not seem to result in mutation, candidate study end points would not include chromosomal abnormalities. Endpoints in which abnormal embryonic growth—such as congenital malformations not associated with chromosomal anomalies, intrauterine growth retardation, and perhaps chromosomally normal spontaneous abortions—is thought to be an underlying mechanism that would be suitable for study. To study the latter group, all abortions would have to be karyotyped, which might be prohibitively expensive.

Exposure assessment is a crucial issue, although it is not clear what the ideal, or perhaps even the most relevant, exposure measure should be. It seems important that both occupational and residential exposures be considered. Community concerns have emphasized the dangers of high tension power lines. Although these exposure sources are less prevalent than many others, they should not be ignored. For research to be revealing, emphasis needs to be placed on developing exposure assessment techniques that are adaptable for epidemiologic investigations of reproductive outcomes and that will not suffer from large measurement errors and consequently reduce our ability to identify positive relations that may exist (e.g., items that can be included in questionnaires and can discriminate levels of field exposures). After more information how a person's exposure changes over time is available, direct measures obtained after the critical period of fetal development may be useful. Consideration of the many methodologic issues discussed above (e.g., sufficient sample size) may allow for greater specificity of findings regarding these common low-level field exposures.

In general, there are many concerns about reproductive health. The possibility that the normal reproductive process may be perturbed by EM field exposures has heightened these concerns further. Given the lack of epidemiologic data to address these concerns and the experimental evidence that certainly does not argue against a possible effect from these exposures, there seems to be sufficient justification for additional study in this area.
