4. Whole Animal Experiments

Animal systems have been examined under a range of electric and magnetic field intensities and for varied exposure conditions and durations. Historically, the animal experiments began by looking for general effects rather than by formulating and testing hypotheses because there was no indication about what system or function, if any, is most likely to be affected by fields.

The very early experiments in this area were riddled with problems of poor experimental design leading to artifacts in results. Because of this, studies prior to 1970 are not discussed in any detail in this report. In the past fifteen years, there have been a set of high quality experiments. But, as in the case of the cellular level experiments, a hypothesis testing stage has not been reached in the science of health effects on animals or humans. Epidemiological studies have focused on a search for cancer because of a historical observation and the public saliency of cancer rather than because cancer is thought to be the most likely effect.

Among the most impressive and concerted set of experiments with animals have been those conducted at the Battelle Pacific Northwest Laboratories in Richland, Washington [Phillips 79] under a rather large project funded primarily by the Department of Energy, and a few smaller projects by Electric Power Research Institute (See Section 8), The first phase of these experiments consisted of extensive screening studies in which animals were examined for all kinds of effects of electric fields at the perceptual, behavioral and physiological levels. This screening was done under fairly high field strengths, much higher than any field that is likely to be encountered even under the right-of-way as it was thought that this would enable a potential effect to be picked up. This argument assumed that exposure to higher fields produce more pronounced effects than that to lower values. The Battelle studies used small animals such as mice, rat and miniature swine to study effects of fields on behavior, physical and motor development and growth, immunology and hematology, and endocrinology. Several of the studies spanned generations. The breadth of these studies, their careful experimental design and interpretation make them the central source of knowledge in this area. This has in large part been due to the excellent team work by experts in the various fields relevant to this area of study such as neurochemistry, stress physiology, psychology, developmental toxicology, electrical engineering and physics and careful integration of the results. Animal studies with sufficient numbers of animals to get statistically significant results, are very expensive and time-consuming. For example, some of the Battelle studies spanned two or three generations of mice and pigs (4-5 years), and involved as many as two hundred rodents in each study.

Other laboratory studies with whole animals have involved isolated experiments rather than an extensive program. Most of these have been funded by the New York State Power Lines Project (NYSPLP), and by the Department of Energy program described in Section 8. Examples are neuroendocrine studies by Michelson et al., circadian rhythm studies on rats by Ehret et al., and on monkeys by Sulzman et al.; on field avoidance behavior of rats by Sagan et al., by Lovely and by Hjeresen et al.; on central nervous system effects by Thomas et al. and Ossenkopf et al.; and development in rats by Walker et al. and Salzinger et al. References are given below as each study is described. Several studies among these were funded by the five-year long New York State Power Lines Project. We have not described the avoidance behavior studies because it is not clear that they have relevance to health effects, especially in humans.

Most well-designed animal studies expose the experimental animal to the fields according to a set protocol of field exposure in a controlled environment. Exposure chambers for the experiments have to be specially developed and calibrated. great care must be **taken** to avoid factors such as vibration, hum, ozone or shock which could lead to erroneous results or “artifacts”. Exposed animals are compared with animals living in an identical environment but subjected only to a “sham” exposure, **that** is, **all** conditions for exposure are simulated but there is no actual exposure. The Battelle studies and some of the others were done “blind” so that the persons handling and recording results from the animals did not know which animals were really exposed and which were sham-exposed.

Field studies have been done on cows and some small animals in Sweden and Italy and by the Bonneville Power Administration in Oregon.

Some studies of human physiological parameters have been done as part of the New York State Power Lines Project. These are outlined in **a** separate section below. Finally, there are several epidemiological studies that have investigated an association between ELF field exposure and cancer. These are discussed in Section 6.

The animal and human studies are now reviewed under the following categories of effects:

1. General effects such as detection, avoidance and behavior responses and development and learning of animals, and moods of humans.
2. Effects on externally measured physical parameters such as growth and birthweight, respiration, heartbeat rate, and temperature rhythms.
3. Effects on specific biochemical such **as** hormones, and blood components
4. Effects on reproduction, growth and development
5. Effects on circadian rhythms of animals and humans.
6. Effects on human perception, performance on specific tests and physiology
7. Epidemiology of cancer, particularly leukemia and brain cancer.

4.1. Detection, Behavior, Learning and Avoidance Responses in Animals

Early Russian reports of necrologic symptoms such as headache and fatigue [Korobkova 72] together with the supposition that nervous tissue might be most responsive to field exposure because some of its functions are enabled through electrical signals, prompted several of the animal experiments. These experiments studied central nervous system (CNS) function directly by the observation of behavior or indirectly by measurements on the secretion of certain hormones known to be associated with effects on the central nervous system.

Perhaps the largest set of behavioral studies have involved studies of animal preferences to remain in or avoid strong electric fields [Hjeresen 80, Stern 83, Stern 85]. While they are interesting, and show, for example that rats can detect fields of just over 1 kV/m, we do not believe these experiments provide much insight on health effects. They do, however, suggest that effects observed in experiments involving strong electric fields may reflect the effects of sensory stimulation, rather than the direct effects of fields on the cell.

Rogers and Smith have conducted experiments on the behavior of baboons in strong electric fields of 30 kV/m and 60 kV/m. While the baboons exhibited alterations in postures and positions, there appeared to be no consistent trend and the changes in positions were noted to be temporary. [Rogers 87]

No perception mechanism for magnetic fields at ambient strengths is known .

Thomas, Schrot and LibOff [Thomas 86a, Thomas 86b] studied the effects of magnetic fields alone or in combination with drugs on specific learning schedules of rats. The objective was to look for effects on behavior and learning and to see if fields affect the action of certain drugs on these animals. Magnetic fields of 0.5, 1, 3 and 5 gauss were used, alone or in combination with 1 kV/m electric field. The results indicate no systematic effect on the behavioral pharmacology of the two drugs used. Both of the drugs have very definite reproducible effects on the learning schedules used. In 60 Hz magnetic fields alone or in combination with electric fields, the learning schedule effects of the drugs continued to be the same as in the absence of the field.

However, when the 60 Hz magnetic field was combined with a static magnetic field, a systematic reproducible modification was produced in one of the learning effects. The change is transitory, lasting more than one hour, but disappearing within 24 hours even when the field exposure is continued. The authors conclude that under very precise conditions, magnetic fields may have an effect on learning.

Ossenkopp and Kavaliers showed that exposure to 60Hz magnetic fields in the range 1 to 1.5 G produces a significant reduction in epileptic seizures induced in rats by pentylenetetrazol, an epileptogenic drug [Ossenkopp 86]. There is no effect **at** 0.5 and 1.85 G. Exposure to 1G also had a weak inhibitory effect on development of seizures by electrical kindling, that is, bringing on epileptic seizure by applying an electric current to the brain. Mice exposed to magnetic field in the range 0.5 to 1.5 G also exhibited significantly less analgesia than control or sham-exposed groups when morphine was administered to them. That is, exposure to magnetic field appeared to make the rats less sensitive to the numbing effects of morphine. The degree of inhibition increased for higher fields. However, the fields did not influence the tolerance development to morphine in the mice.

These observations can not be simply extrapolated to any general conclusion except to note that there are central nervous system effects which may be windowed even in the whole animal, and be very specific with respect to field values as well **as** to specific functions.

4.2. Effects on Hormone Levels and the Central Nervous System

Levels of specific hormones are maintained in balance for the proper functioning of the central nervous system (CNS) (See Endnote 2 for discussion of the specific hormone systems). Most prominent among the aminoacid hormones synthesized in the brain and the nervous system are the catecholamines dopamine, norepinephine and epinephrine. As they **are** released from nerve endings during physiologic stimulation, they are called neurotransmitters. They have several functions and affect muscle, heart, liver, spleen, lung and brain physiology. They control blood pressure, heartbeats, some forms of headache, the basic metabolic rate, some psychological changes and **several** other rates. Deficient or excessive secretion of catecholamines or alterations of their action cause major physiological and psychological problems. Increased metabolism of catecholamines is also associated with neuroblastoma, a tumor originating in the neural crest, often during fetal development.

Serotonin stimulates or inhibits many of the muscles and nerves, depending on the amount and the phase of the organ in its function. it can stimulate or depress heartbeat, contract blood vessels and change blood pressure. Serotonin prevents clotting, and provides reflexes such as coughing or hyperventilation. In humans, serotonin also serves as a chemical transmitter in the brain. Serotonin and its product melatonin influences sleep, perception of pain, psychological depression and social behavior. Melatonin is also secreted by the pineal gland and is described in the endnote on circadian rhythms.

The levels of these hormones are not only responsive to external and internal signals, but undergo a regular pattern of variation in different periodic rhythms. One such rhythm is the circadian rhythm which has a period of about 24 hours (See endnote 4 on circadian rhythms). Large variations of these levels and rhythms are therefore indicative of perturbations of CNS function.

In a study at Battelle, Free et al. (1981) noted a phase shift of the normal variations of hormones in adult male rats exposed to 64 kV/m for 30 days and 120 days, but no change in body or organ weights. They concluded that continuous exposure to electric fields may alter some endocrine system secretions but do not appear to impair normal physiology [Free 81]. No significant changes were noted in the levels of various neuroendocrine secretions by rats for 1 or 3 hours at 100 kV/m by Quinlan et al. [Quinlan 85].

A pineal function change was seen in the Battelle studies by Wilson et al. (1981). Continued exposure to 60Hz electric fields of 1.7 to 65kV/m produced a depression of the night-time levels of melatonin in rats, and introduced a delay in the activity in the rhythms of other biochemical activity. This pineal melatonin depression effect did not appear in the animals immediately on exposure. For a 39 kV/m field, the onset of the effect appears after two and before three weeks of exposure. In less than three days after the cessation of exposure, the levels returned to normal. This experiment is discussed again in the section on circadian rhythm because of its importance in that context.

Investigating this delay in the secretion of the neurochemicals in detail, Vasquez and coworkers working jointly with the Battelle group, have found that the daily periodicity (or, circadian rhythm) of some pineal hormones such as melatonin undergoes a change in rats exposed to strong electrical fields. A period shift of four hours has been observed for the hormones norepinephrine, serotonin and dopamine in the exposed rats. [Vasquez 86]. This shift in the time of occurrence of peak and low levels, called “phase shift”, may or may not be present in humans. **A** phase shift of these hormones with respect to the natural light-dark cycle, if present in humans, might have implications for certain psychological disorders of biochemical origin such as sleep and mood disorders, and chronic depression. As described in Section 5 (Figure 5-1), the fields in these experiments generate in the animal a current density comparable to the exposure situation in a home near a 500kV line.

CNS endocrine secretion effects were also seen by Wolpaw et al. in an experiment on pig-tailed macaque monkeys [Wolpaw 87].. The animals were exposed to electric and magnetic fields from (3 kV/m and 0.1 G) to (30 kV/m and 0.9 G) for three periods of 21 days each, with 21 days of sham exposure in between. Weight, blood chemistry, blood counts and performance on a simple motor task as well as postmortem examination of brain and organs showed that fields did not apparently affect any of these factors significantly for the period of exposure. Spermatogenesis was also seen to be normal. The monkeys viewed by videotape while in the fields showed no indication of disturbance.

Cerebrospinal fluid examination at the end of each period showed significant decline of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) whose levels in turn reflect those of dopamine and serotonin (See endnote 2 on hormones). The experiments did not show any circadian shifts. The 5-HIAA concentration failed to return to original levels after exposure, showing a permanent effect in modulating an important neurotransmitter system which also plays a role in several psychochemical disorders as mentioned above.

4.3. Effects on Blood and Immune System Chemistry

Blood and serum chemistry can reveal abnormal levels of metabolizes, immune system components or hormones which may be indicative of improper functioning of some organ system. Blood chemistry of rats exposed continuously to unperturbed fields has been examined in several studies.

A Battelle study looked at specific components of the immune system in mice in 68 kV/m fields for 30 to 150 days. It found no systematic significant variation in counts of blood cells or antibody responses [Morris 82]. In another study at Battelle, adult rats were exposed for 15,30,60 or 120 days to a field of 68 kV/m. Blood counts of cells necessary for proper immune responses as well as serum constituents indicative of proper level of metabolism were studied in detail in replicated experiments on groups of rats. No variation was observed between exposed and sham-exposed rats in the various parameters examined [Ragan 83]. Studies on immune response of rats at a field level of 100kV/m also showed no effect [Morris 87]. In independent experiments, Michelson et al. at the University of Rochester also found no change in these parameters [Quinlan 85]. The experiments on monkeys by Wolpaw et al. mentioned in the preceding section also showed normal hematology and serum chemistry.

These experiments imply that there is no general or overall immune system performance changes or endocrine system changes induced by exposure to electric fields of a rather high intensity over a duration of several months.

4.4. Effects on Reproduction, Growth and Development

Reproduction, growth and development studies measure a wide variety of factors including: reproductive behavior such as mating and fertility; the viability of the fetus; alterations in physical parameters such as birth weight and head size; gross malformations; and central nervous system development. In addition, some experiments have studied adult growth, particularly of bones and the ability of bone to repair after it has been fractured. These are now discussed under the different categories of reproduction and pre- and perinatal external development; central nervous system development and adult growth and repair capability as examined under field exposure,

Reproduction, prenatal and perinatal development

Most of the studies of possible developmental effects of ELF field exposure have concluded that there are no overt defects and malformations as a result of exposure. However, some studies have seen subtle effects and the possibility of the existence of effects remains an open question. Tables 4-1 and 4-2 summarizes the experimental results.

Several investigators have used chicken eggs to study the effect of ELF fields on embryonic development. While early experiments in Spain, using pulsed[12] magnetic fields reported an increase in developmental abnormalities [Ubeda 83, Delgado 82], attempts to replicate the effects yielded mixed results. Tell and coworkers at the U.S. Environmental Protection Agency could not see any statistically significant effect [Martucci 84]. However, Mild reported from Sweden that he did observe an increased abnormality in chick embryos exposed to weak, pulsed magnetic fields [MWN 84]. Maffeo et al. also found no developmental effects on chick embryos exposed to pulsed ELF fields [Maffeo 84].

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[12] Pulsed fields are fields which are turned on quickly for only a brief period.

Table 4-1: Summary of reproduction, prenatal and perinatal development in rats, and chicks exposed to 60Hz fields

Animal and Exposure Conditions	Observed Effects and Conclusions
Chick eggs incubated in 0-100kV/m electric fields	No effects on mortality, deformity or birth weight. No physical developmental defects in chicks due to exposure in this range
Rats in 100kV/m fields	
Males and females exposed	No effect on mating performance or fertility
Females exposed during pregnancy	No effect on full-term development of appearance and size of fetus
Females exposed during pregnancy; exposure of new-born continued for 8 days	No effect on litter size, stillbirths, birth weights, or early external neuromuscular or neurological development
Fetal exposure beginning at three-fourths term to 25 day old newborn	Fewer stillbirths and neonatal deaths in exposed compared to sham-exposed animals. No observable changes in early neonatal development

Todate, exposure to 60Hz fields of chick embryos has not shown any significant abnormalities. Graves et al. [Graves 85] exposed over 20,000 eggs to a range of 60 Hz electric fields ranging from O to 100 kV/m through the 21-day incubation period. They found no effects on mortality, deformity, or on weights of embryos or one-day old chicks.

Pulsed magnetic fields, however, continue to cause concern and controversy in the scientific community with respect to their potential detrimental effect on the development of chick embryos. Following the early work cited above, the U.S. Office of Naval Research and the U.S. Environmental Protection Agency sponsored six independent laboratories in the U. S., Canada and Europe in a planned series of experiments involving exposure of chick eggs to pulsed magnetic fields with the same set of characteristics. All the laboratories also examined the same endpoints. Exposed eggs were examined for fertility. Embryos were examined for abnormalities in development, and for growth. This project, nicknamed the “Henhouse Project” showed an overall increase in the proportion of abnormal embryos in the exposed group for all the laboratories taken together, although the exact proportion of abnormality differed from one laboratory to another. It is to be noted again that this result is for pulsed fields. Scientists cannot say what the implications are for 60Hz fields and humans. The Henhouse Project group are planning further research on developmental abnormalities.

Three experiments of reproduction and development were done on large numbers of rats (over 100 rats in each study) as part of the early screening studies at Battelle. The animals were exposed to uniform 100 kV/m 60 Hz electric fields [Phillips 79].

The first experiment, replicated three times, examined reproductive behavior, fecundity and fetal development. The male and female animals were exposed to the field for six days. This did not affect their reproductive performance. A 30-day exposure of males and females prior to mating also did not affect mating performance or fertility. The females continued to be exposed during pregnancy. The appearance and size of fetuses were examined after 20 days of gestation (Full term for rats is about 22 days). In the second experiment, postnatal development subsequent to prenatal exposure was examined in four replicates. Exposure was begun on the first day of pregnancy and continued until the offspring were 8 days old, a total of 30 days. Parameters of physiological, behavioral and neuromuscular development were noted. Exposure did not affect litter size, incidence of stillbirths, or birthweights. No differences between exposed and sham-exposed animals were noted in morphological, neuromuscular or neurological development.

The third experiment of five replicates measured development as a consequence of exposure for 30 days, from day 17 of gestation to when the offspring was 25 days old. The same set of developmental measures as in the previous experiment were used. Significantly fewer stillbirths and neonatal deaths were noted in the exposed group in this case. No changes were noted in neonatal development.

The authors concluded from these experiments that exposure to high fields before and immediately after birth did not affect the growth or development of rats.

Two experiments in which rats were exposed prenatally to 80 kV/m fields during the last trimester of pregnancy indicate that such exposure may slightly retard postnatal development as measured by ear flap separation and eye opening and alter sexual differentiation. These experiments were, however, done using only about 15 experimental and 15 control animals each and the results are therefore are not conclusive. [Burack 84]

A study of Hanford miniature swine was also a screening study to look at a larger and longer-lived species than rodents over multiple generations. The time course of the systematic study over three generations is shown in Figure 4-1 reproduced from the paper by Sikov [Sikov 87].

In the figure, F_o denotes the original generation of the female swine. These lived in a 30 kV/m, 60 Hz electric field for 20 hours each day for 4 months before they were mated with unexposed male swine, and continued living in the field while they were pregnant with the first, and in some cases with the second, set of offspring. The first generation F, females were bred to unexposed boars at 18 months of age and gave birth to the second generation F_2. In the figure, Teratology[13] I,II, Ill denotes the points in time at which detailed morphologic evaluations of the newborn were performed. This included external measurements, weight and observations of internal and external malformations. Prenatal embryonic loss was also noted.

Teratology I and Ill, of the first set of offspring of the original and of the second set of offspring of the first generation yielded no incidence of abnormal growth or malformations as compared with sham exposed swine. Teratology II of the second bred offspring of the original generation showed a significantly larger proportion of malformations than the corresponding sham-exposed group.

There was a tendency toward less prenatal mortality in the exposed group. That is, there were more live fetuses per litter in the field-exposed group than in the sham-exposed. There were no other significant differences. The authors conclude that while the experiment suggests that there is an association between field exposure and prenatal growth and development, no definite conclusions can be drawn.

Two replications of the experiment similar to the swine experiment were performed with rats as a followup to the swine study at Battelle [Rommereim 87]. The rats were exposed to a higher field - 10OkV/m for 19 hours per day. An experimental protocol similar to the swine study over the three generations was used.

In the first of these experiments, an increase in birth defects in the second farrow of the original (F_o) generation and a decreased fertility of the F, generation were noted. But these effects were absent in the second replicate study. Because of this, it is not clear whether the observed effects in the first experiment were due to a random variation rather than due to a significant effect of field exposure.

The scattered positive results in these experiments do not allow the possibility of an association between electric field exposure and gross musculoskeletal abnormalities to be ruled out. However, taken together, the studies do not provide strong support for the existence of an effect.

<u>Prenatal exposure</u> <u>in</u> <u>humans</u>

Wertheimer and Leeper (Wertheimer 87) used birth announcements to examine the association between the use of electric blanket or electrically heated waterbed and irregularities in pregnancy outcomes. The authors noted a seasonal pattern indicating a higher abortion rate, longer gestation periods and lower birthweights in babies born to users of heated waterbeds and electric blankets.

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[13]Teratology is the study of birth defects

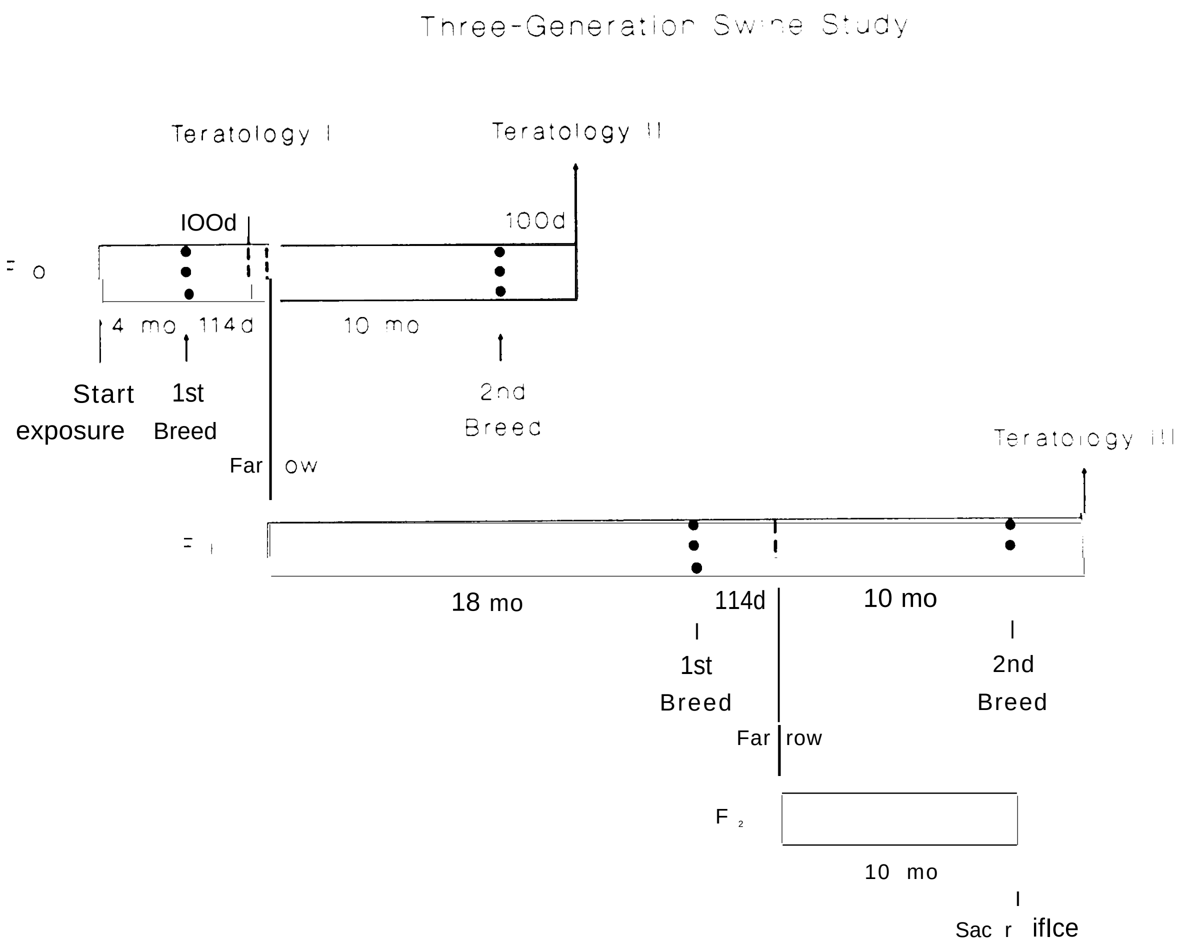

Figure 4-1: Scheme for three-generation reproduction study of Hanford miniature swine exposed to 60Hz electric field of 30 kV/m, 20 hours a day, 7 days a week: The horizontal length of the bars are proportional to the time elapsing in each generation. F_o, F_1, and F_2 denote the original, first generation and second generation of miniature swine respectively. Generations F_0 and F, were bred twice. After the start of the exposure, the female swine continued to live in the electric field. F_0, the original generation consisted of 49 sows derived from 13 mothers and a single father. 31 of these 48 animals formed the exposed group, and 18 the sham-exposed group. The F_0. sows were bred first after 4 months of exposure to unexposed boars. 18 exposed and 10 sham-exposed sows of the F_0 generation produced the F_1 generation. Teratology I (examination for birth defects) was done 14 days prior to birth on some of the litters of the F_0 swine. The F_0 were bred again after 10 months to produce the second farrovv of the original generation. The F, females were bred at 18 months age to produce F_2 generation and again 10 months later to produce the second farrow of the first generation.

Reference: [Sikov 87]

Table 4-2: Studies of Three Generations of Swine and Rats

Animal and Exposure Conditions	Observed Effects and Conclusions
Hanford miniature swine Three generations in 30kV/m electric field Females exposed and mated with unexposed boars	First set of offspring of original and second set of offspring of first generation normal in prenatal development. Less prenatal mortality in exposed group. Second bred offspring of original generation showed increased incidence of malformations primarily of musculoskeletal system.
Rats: Replication of swine study. Two repetitions of three generation study	
Study 1	Increase in birth defects of second farrow of first generation parallel to swine study
Study 2	No effect observed.

This study is at best a preliminary scoping study because of the large number of experimental biases and small sample size. Sources of human prenatal developmental abnormalities are characterized only for at most 20 to 30 % of the observed cases [Wilson 74] and confounding effects abound. Only a very careful study done with a knowledge of the base seasonal variations of different kinds of abnormalities, maternal habits and exposures, and genetic susceptibility can reveal any potential effect of fields on the developing human. A database for the baseline for such a study exists in the Congenital Malformation Surveillance System at the Center for Disease Control in Atlanta [Edmonds 81]. This is an intensive surveillance system which is a useful resource for birth defect studies, especially in the case of weak potential agents such as ELF fields. On our initiative, selected questions related to ELF exposure have been added to the survey questionnaire for this system since late 1985 [Sever 84] and may yield reasonable conclusions by the early 1990's. The questions ask about the use of electric blankets and electrically heated waterbeds during and immediately preceding pregnancy in order to assess if there is any observable association between such use and birth defects.

Growth, development and bone repair in adult animals

Growth and repair in bones have been associated with pulsed ELF fields used clinically [Bassett 74, Bassett 82] and several studies have examined the effects of 60Hz fields on bone growth and repair.

In a large study at Battelle, Hilton and Phillips conducted a series of 31 separate experiments, 17 with rats and 14 with mice to determine effects of 65kV/m fields for different periods of exposure (30, 60, or 120 days) [Hilton 81]. Effects examined were: body and organ weights; food and water consumption; and, metabolic rates such as oxygen consumption and carbon dioxide production. While there were some variations in some of the experiments, the authors concluded that there were no major changes in any of these features and that therefore living in 65 kV/m fields for four months produced no effects on the growth and metabolism of rodents.

A smaller study by Walker et al. [Walker 82] examined effects on bone growth in prenatally exposed rats. Leg bones from 55 adult rats conceived, born and raised in a 80 kV/m, 60 Hz electric field were compared with those from sham-exposed animals. Body weight, wet and dry bone weights, bone length, and specific gravity of bone were studied. Chronic field exposure enhanced growth in the long bones causing increased length and mass, but not in specific gravity. No tumors or other effects were noted. The magnitude of the effect was small, about 5%, but statistically significant. In another study, male rats were exposed to 10.2 G at 60Hz for 30 days . Although there appeared to be a trend toward impaired growth, there were no observable skeletal effects [Simmons 86].

The Battelle group also studied the effect of 10OkV/m fields on bone growth and fracture repair [McClanahan 83] in rats. Exposure of young and adult rats of both sexes for 20 hours a day did not alter growth rate of bones. Bone repair was tested by examining bending and breaking strength of fractured and intact leg bones at several periods after bone surgery. The exposed group showed a slightly lower repair capability as measured by lower strength during early periods after surgery(16 and 20 days), but the repair was normal by day 26. The authors state that the exposure retards the rate of repair but does not lead to permanently diminished strength. It is also not clear whether the diminished repair was due to the lowered rate of bone deposition or due to the fact that the rats in the field tended to move more than the sham-exposed rats because they felt the field.

Overall, high intensity electric fields do not appear to have a strong effect on bone growth and repair in rodents.

Early brain and central nervous system development

There are several isolated experiments that have looked at different effects which are indicators of early development of the brain and central nervous system. Because of the different aspects examined, they do not lead to any simple conclusion. The results are summarized in Table4-3. The one significant lesson from these experiments is that there maybe subtle effects in facets of development that are hard to measure. These may include learning retention as the animal is subjected to repeated learning experiments. All but one of the studies have done single measurements of some parameter of learning rather than continued repetitive learning.

Studies in Sweden by Hansson reported that the brain morphology of certain parts of the brain of various small animals such as rodents and rabbits born and reared under 100 kV/m fields showed abnormalities [Hansson 81]. These results were based on qualitative tissue pathology and were subject to significant criticism in the research community. Experiments since then have failed to replicate the result [Albert 84].

As part of the New York State Power Lines Project (NYSPLP), a study by Gona et al. examined the various aspects of the developing nervous system in rats [Gona 871. The prenatal and perinatal development of rat brain was studied under continuous exposure of pregnant and newborn rats. Three field combinations (1 kV/m and 10 G); (100 kV/m and 1 G); and, (100 kV/m and 10 G) were used. Indexes of cerebral and cerebella development of the brain were noted for different periods of development.

No significant permanent differences in the biochemical and morphological parameters of brain development were observed between exposed and sham-exposed animals. The features observed by Hansson were not evident in these animals.

Blackman et al. [Blackman 88] examined whether the in vitro calcium efflux effect in chick brain tissue described earlier in section 3 is affected by prenatal exposure of the chick. (i.e., the exposure of eggs) to 60 Hz and 50 Hz fields. They found that eggs exposed to a 60 Hz electric field produced chicks with brain tissue that showed the calcium efflux effect for 50 but not 60 Hz. Eggs incubated at 50 Hz produced chickens with brain tissue that were not affected by 50 or 60 Hz fields. The result was not sensitive to particular intensity values, but to the frequency. This finding was confirmed in three separate experiments by Blackman. It shows that prenatal exposure to ELF fields can affect postnatal tissue physiology in very specific ways.

Subtle central nervous system effects can result from some prenatal insults that may be manifested only later in the offspring's life and hence may not become evident in studies done soon after birth. Examples of prenatal chemical insults that lead to defects much later on in life are the pregnant mother's use of diethylstilbesterol (DES) which led to carcinogenesis in women offspring; and of alcohol use that can lead to learning deficits in children and nutritional deficits that lead to persistent functional deficits [Snell 82].

The Battelle studies described earlier in this section have examined some learning and behavioral

Table 4-3: Early development of brain and central nervous system in exposed animals (Details in text)

Experimental Conditions	Observations and Conclusions
Rodents and rabbits born and reared in 10OkV/m; Brain tissue examined for change in appearance	Alteration noticed on examination by Hansson in Sweden. Attempts at replication by Albert in the U.S. found no evidence of the differences.
Prenatal and perinatal development under combinations of 1 kV/m and 100kV/m electric field, and 1G and 11 G magnetic field	No significant effects on biochemical or visual morphology of brain development
Calcium efflux effect in brain tissue of chicks hatched from exposed eggs	Frequency window may be affected by prenatal exposure. No intensity window
Rats exposed from 3/4 term of gestation to 11-20 days age	No effect on early motor activity learning; No effect in total electrical activity of the brain
Early learning and repetition of learning in rats exposed in utero	Learning response decreases when learning tests are repeated.

aspects of newborn rats as well as perinatally (day 11-20). In the simple learning experiments involving motor development, no significant effects were found.

in another set of experiments at Battelle, Jaffe [Jaffe 83] measured the development of the visual evoked response (VER) in newborn rats exposed prenatally and perinatally. The VER is a measure of the total electrical activity of the nerve cells that process the information supplied by a visual stimulus (regular light flash in this instance). Early changes are an index of CNS development. In tests on a total of 114 rats from 114 litters, no significant effect of exposure was found for upto 20 days of perinatal exposure.

Salzinger et al. note that it may be important to study behavioral effects over more training sessions than may be done ordinarily [Salzinger 87]. In their studies, they examined the behavior of rats exposed in utero and for the first eight days of life. Exposure levels of 30 kV/m, 1 G and 10 kV/m, 0.33 G fields were used and the experiment was done blind, with sham and real exposure settings.

A specific behavioral and learning test was used. Other parameters such as physical appearance, general activity level and weight were also monitored. None of the physical parameters showed any difference between the sham and exposed groups at either of the field levels. The exposed and sham-exposed group started out with the same learning response level. However, repetition of the learning tests showed that the performance of the two groups increasingly diverged, with the exposed group showing a more and more lowered rate of response in subsequent sessions. This divergence was higher for the higher field levels than the lower. This difference in learning was found to be robust in that it was maintained when the behavior was extinguished and the animals reconditioned. The effect was reproducible.

Salzinger et al. note that most experiments involve an examination of the early learning behavior and do not continue conditioning studies. Their results show that it is important to study conditioning over a larger number of training sessions because the effects may become evident only late in the conditioning process. The robustness of their results implies that it may be important to attempt to replicate experiments of this type in other laboratories, in other animals and for other learning behaviors in order to understand the full implications of perinatal field exposure for learning.

4.5. Effects on the Circadian Systems of Animals and Humans

The circadian timing system serves to synchronize various physiological and biochemical processes that have a daily cycle. While many aspects of the biology of the circadian and other timing systems are not well understood as yet, the last two decades have brought considerable understanding of some of the elements of the system. Endnote 4 summarizes some of the relevant background and terminology.

Early work by Brown [Brown 70] suggested that geophysical variables (timing and amount of sun, etc.) play an important role in giving time cues to circadian systems. Natural geomagnetic and geoelectrostatic fields maybe one of these entraining cues as they undergo a daily variation of about 15% in intensity. Dowse and Palmer [Dowse 69] showed that an electrostatic field can entrain the activity rhythm of mice.

Wever's is the only extensive work on the effects of low intensity fields on circadian activity of humans [Wever 74, Wever 79]. Human subjects (all men) lived in underground bunkers for 3 to 8 weeks at a time. One bunker was isolated from natural electromagnetic fields while one was not. Subjects living in the shielded bunker showed **a** tendency to have desynchronized temperature and activity rhythms, with significantly longer circadian periods than those who continued to be exposed to the natural fields. The application of a small electric field of 2.5 V/m at 10 Hz reduced the internal desynchronization, while a 600 V/m direct current (DC) failed to have any effect. Application of the low-intensity, low-frequency field in 12-hour on, 12-hour off cycles restored the circadian period to the natural value.

Work by Ehret's group at the Argonne National Laboratories monitored different rhythms of mice simultaneously while exposing them to different AC fields [Duffy 82, Ehret 80]. Their work showed that depending on the field applications protocol, phase delays were produced in activity and metabolism rhythms. However, as the field strength used in this work **was very** high (130kV/m) and only one species of mice were used, the work can not be used to conclude that lower field levels affect circadian activity in rodents.

Dowse (1982) also showed that a 150 V/m electric field at 10 Hz advances the phase in the locomotor activity of the fruit fly Drosophila Melanogaster under constant light conditions when the field is applied in a 12-hr on, 12-hr off pattern, perhaps taking the place of the normal LD cycle cue.

The most striking and directly demonstrated circadian effect of 60 Hz electric fields on animals came from the work of Wilson, Anderson and colleagues at the Battelle Pacific Northwest Laboratories. They examined the effect of continued 60 Hz electric field exposure on the functioning of the rat pineal gland as measured by the circadian pattern of secretion of 5-methoxytryptophol (5-MHOT, melatonin and serotonin-N-acetyl transferase (SNAT). Night levels of melatonin and SNAT in mice are generally several times higher than day levels. Field exposure in the range of intensities 1.7 to 65 kV/m depressed the melatonin rhythm , and introduced a delay in the SNAT activity rhythm. This effect, however, was not immediate on field exposure . For a 39 kV/m field, the onset of the effect appears after two weeks and before three weeks of exposure. The animal recovers from the effect on cessation of exposure in less than 3 days after initiation of exposure. There was no apparent change in the magnitude of the effect at the different field strengths.

As part of the New York State Power Lines Project, Sulzman and colleagues examined the effects of a range of electric and magnetic fields (O to 39 kV/m, O to 1 gauss) on free-running periods of food and oxygen consumption of squirrel monkeys, maintained under constant light [Sulzman 86]. Although the number of monkeys used in the experiment is small (1 O), there was a systematic increase of effect with increasing values of field intensity. The two rhythms did not show any increase in a 2.6 kV/m, 1 G field; Three out of nine monkeys showed a statistically significant increase in the period of both rhythms in **26** kV/m, 1G; and three out of four monkeys showed an increase in a 39 kV/m, 1G field. There was no desynchronization between the two cycles measured . Both individual variation of susceptibility to the effect among the monkeys and residual effects were noted. Three of the ten monkeys involved in these experiements continued to maintain their longer period even after the removal of field exposure. Inspite of the small number of animals in the experiment, the results are reliable because the investigators have maintained several years of circadian period data on this class of monkeys and found them to be remarkably stable with little dependence on age and various kinds of treatment.

In summary, experiments on the effect of electric and magnetic fields on the circadian systems of man, primates and lower animals indicate a definite effect of 60 Hz fields on the periodicity of physiological functioning. It is not clear whether such effects are deleterious or even long-lasting. Dyschrony of the circadian system has been associated with physiological and psychological disorders ranging from altered sensitivity to drugs and toxins and internal conflicts between the timing of physiological processes to sleep, performance and other psychiatric disorders including chronic depression [Maurizi 84]. Hence it would be useful to do some careful and focused research on the potential effects of low-level 60Hz fields on the circadian system in humans and animals.

4.6. Experiments with Human Subjects

Like many other animal species, humans can detect power-frequency electric fields through stimulation of receptors on the surface of the skin. Deno and Zaffanella [Deno 82] found the threshold of perception to depend on body posture and to vary markedly across individuals. The lowest detection thresholds for vertical electric fields were associated with stimulation of hand hair with the hand held over the head. The median threshold of perception across 136 individuals for this posture was found to be 7 kV/m. With arms at the side, the field is first perceived as stimulation of head hair. The median threshold of perception in this case was about 23 kV/m. For both postures, the most sensitive individuals could detect fields smaller than 2 kV/m.

In a carefully designed experiment, Graham et al. conducted a study to evaluate human perception, performance and physiology in 60 Hz electric and magnetic fields. The effect of fields on performance was studied through a specific battery of tests that measured effects on the EEG[14] in response to visual and auditory signals; memory; reaction time; time perception and some specific information processing abilities. Physiology was monitored by blood chemistry and other parameters such as heart rate. Subjective feelings were also elicited [Graham 871. The exposure chamber was carefully designed and built, and the study done blind with each volunteer subject serving as his own control. All 20 subjects were healthy males between 21 and 35 years of age, and were given complete explanation of the purpose of the experiment. Field strengths were O-32 A/m and 15 kV/m for a few hours at a time.

The perception experiments showed that while subjects differed in their sensitivity to the fields, there was no difference when the fields were presented individually or in combination. Fields increasing gradually resulted in a higher perception threshold than a sudden onset.

Most vital signs, physiological parameters, daily life activities and moods were not affected by the field strengths presented. Also not affected were simple reaction time, memory span, fatigue and ability to make decisions. Some changes were detected in heart beat interval and on tests demanding specific EEG activity but the variations were within normal ranges for these parameters.

Followup studies of the observed heartbeat changes showed some definite effects in heartbeat rate and performance. Two groups of fifteen subjects each were exposed to different exposure conditions. One group was subjected to field exposure for 6 hours in alternating 45-minute periods of field on and off. The second group was exposed to a fast, intermittent exposure pattern of 15 seconds of switching on and off for periods of 45 minutes followed by 45 minutes of fields off. While preliminary, the results suggest

[14]The EEG or electroencephalogram, is a record of the variations in electric potential recorded from the brain and is indicative of the electrical activity in the brain. EEG patterns depend upon diverse factors such as age, sleep state, blood glucose, and levels of brain hormones.

that alertness and reaction time were notably affected in the intermittent exposure group and there is an individual variation in individual susceptibility to fields. [Graham 88]