MINIREVIEW

Biological Effects of Power-Frequency Fields As They Relate to Carcinogenesis

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JOHN E. MOULDER*,[1] AND KENNETH R. FOSTER†

Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin 53226 and Department of Bioengineering,† University of Pennsylvania, Philadelphia, Pennsylvania 19104*

Abstract. **There is a widespread public perception that exposure to electricity is linked to cancer. The public concern stems largely from epidemiological studies which appear to show a relationship between cancer incidence and exposure to power-frequency electromagnetic fields. This review will discuss the biophysics of power-frequency electromagnetic fields as it relates to biological effects, summarize the current state of the cancer epidemiology, and then concentrate on the laboratory studies that are relevant to addressing the possibility that power-frequency fields are carcinogenic.**

Review of the epidemiological evidence shows that the association between exposure to power-frequency fields and cancer is weak and inconsistent, and generally fails to show a dose-response relationship. The laboratory studies of power-frequency fields show little evidence of the type of effects on cells or animals that point towards power-frequency fields causing or contributing to cancer. Finally, from what is known about the biophysics of power-frequency fields, there is no reason to even suspect that they would cause or contribute to cancer. Application of "Hill's criteria" to epidemiological and laboratory studies shows that the evidence for a causal association between exposure to power-frequency fields and the incidence of cancer is weak.

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There is a widespread public perception that exposure to electricity is linked to cancer. Most of the concern about electric power and cancer stems from epidemiological studies which appear to show a relationship between exposure to power-frequency magnetic fields and the incidence of cancer. The first of these studies, published by Wertheimer and Leeper (1) in 1979, reported a relationship between residence near certain types of powerlines and the incidence of childhood leukemia and brain cancer. This was followed in 1982 by reports from Milham (2) and Wright *et al.* (3) that workers in "electrical occupations" had a higher than expected incidence of leukemia. Over 100 epidemiological studies have followed, some of which report that excess cancer, particularly leukemia and brain cancer, is associated with exposure to power-frequency fields. These reports of excess cancer have been met with considerable skepticism in the scientific community, in part because few were based on actual measurements of fields, and in part because of the absence of plausible mechanisms through which these fields could cause or contribute to cancer.

This review will discuss the biophysics of power-

[1] To whom requests for reprints should be addressed at Radiation Oncology, Medical College of Wisconsin, 8700 West Wisconsin Avenue, Milwaukee, WI 53226.

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frequency fields as it relates to biological effects, summarize the current state of the cancer epidemiology, and then concentrate on the laboratory studies that are relevant to addressing the possibility that power-frequency fields are carcinogenic.

Biophysics of Power-Frequency Fields

x-rays, ultraviolet (UV) light, visible light, microwaves (MW), radiofrequency (RF) energy, and electromagnetic fields from electric power systems are all parts of the electromagnetic (EM) spectrum, and are characterized by their frequency or wavelength. The frequency is the rate at which the EM field changes direction, and is usually given in Hertz (Hz) where 1 Hz is one cycle per second. In an EM wave, the frequency (f) and the wavelength (λ) are related by the equation:

$$\lambda = (\text{speed of light})/f$$

so that as the frequency rises the wavelength gets shorter. Electric power has a frequency of 50 Hz in most of the world (60 Hz in the United States) and a wavelength of about 5000 km. By contrast, AM radio has a frequency around 10^6 Hz and a wavelength of around 300 m; MW ovens have a frequency of 2.54×10^9 Hz and a wavelength of about 12 cm; and x-rays have frequencies of over 10^{15} Hz and wavelengths of 100 nm or less.

Terminology. We will use the term "power-frequency" to refer to both the 50- and the 60-Hz alternating current (AC) frequencies used in electric power systems, and the term "power-frequency field" to refer to the sinusoidal electric and magnetic fields produced by 50- and 60-Hz lines and devices. The phrase "EMF" will be avoided since it is an imprecise term which could apply to many very different types of fields, and because the term has a long-standing usage in physics to refer to an entirely different quantity, electromotive force. We will also avoid the terms "electromagnetic radiation" and "nonionizing radiation" since power-frequency sources produce no appreciable radiation. Power-frequency fields are also properly referred to as extremely low frequency (or ELF) fields, a broader term often used to cover the range from >0 Hz to 3000 Hz (4).

Fields Versus Radiation. In general, EM sources produce both radiant energy (radiation) and nonradiant fields. Radiation travels away from its source, and continues to exist even if the source is turned off. In contrast, some electric and magnetic fields exist near an EM source that are not projected into space, and that cease to exist when the energy source is turned off. Powerlines are far too short compared with the wavelength of 50/60-Hz radiation (5000 km) to be effective radiation sources. While powerlines theoretically radiate some energy, they do so with such low efficiency that this effect can for all practical purposes be ignored.

Magnetic Versus Electric Fields. The fact that exposure to power-frequency fields occurs at distances that are much shorter than the wavelength of 50/60-Hz radiation has important implications, because under such conditions (called "near-field"), the electric and magnetic fields can be considered independent entities. This is in contrast to EM radiation, in which the electric and magnetic fields are inextricably linked.

Electric fields exist whenever electric charges are present, regardless of whether current is flowing; their units in the SI system are volts/meter (V/m). Magnetic fields are produced by moving charges (e.g., current flowing through a conductor); their units in the SI system are amperes per meter (A/m). For historic reasons, it is more common to specify magnetic fields using a different quantity, the flux density, whose units in the SI system are Tesla (T). Another unit of flux density, often used in the United States, is the Gauss (G), where 10,000 G equals 1 T (1 G = 0.1 mT = 100 μT).

The magnetic fields associated with powerlines, transformers, and appliances easily penetrate buildings or tissue and are difficult to shield. By contrast, power-frequency electric fields are easily shielded by conductive objects and have little ability to penetrate buildings or tissue. Because power-frequency electric fields do not penetrate the body, it is generally assumed that any biologic effect from routine exposure to power-frequency fields must be due to the magnetic component of the field, or to the electric fields and currents that these magnetic fields induce in the body.

The strength of an electric field is proportional to the voltage of the source and its distance to the observer. Thus, the electric fields beneath high-voltage transmission lines far exceed those below the lower-voltage distribution lines. The magnetic field strength, by contrast, is proportional to the current in the lines, so that a low-voltage distribution line with a high current load may produce a magnetic field that is as high as some high-voltage transmission lines. In fact, electric distribution systems account for a far higher proportion of the population's exposure to magnetic fields than the larger and more obvious high-voltage transmission lines.

Typical Field Intensities. Within the right-of-way of a high-voltage (115–765 kV) transmission line, fields can approach 10 μT and 10,000 V/m. At the edge of a transmission right-of-way, the fields will be 0.1–1.0 μT and 100–1000 V/m. Ten meters from a 12-kV distribution line, fields will be 0.2–1.0 μT and 2–20 V/m. Actual electric fields depend on design and voltage, and since the voltage of a line is closely regulated, the resulting electric fields are essentially constant. By

contrast, the magnetic fields depend not only on voltage and design, but also on current load, and thus can be highly variable from day to day, and even within a day.

Fields within residences vary from over 200 μT and 200 V/m a few centimeters from appliances that contain electric motors, to less than 0.02 μT and 2 V/m in the center of some rooms (5).

Exposures in excess of 100 μT and 5000 V/m have been reported for workers in some occupations (e.g., arc welders and electrical cable splicers). However, in typical occupations whose job titles imply exposure to power-frequency fields, mean exposures are 0.5–4 μT and 100–2000 V/m (5). Indeed, the magnetic field exposure of workers in many of these "electrical" occupations is little different from that of other individuals.

Interactions of Electromagnetic Sources with Biological Material

The nature of the interaction of EM fields and radiation with biological material depends on the frequency of the EM source; and for reasons discussed below, the known mechanisms through which ionizing radiation, optical radiation, RF, and MW affect biological material have no relevance for power-frequency fields. Although we usually discuss EM sources as though they produce waves of energy, sometimes EM energy acts like particles, particularly at the higher frequencies. The particle nature of EM energy is important because it is the energy per particle (photon) that determines whether EM energy can directly affect chemical structure.

Direct Effects. At the frequency of vacuum-UV and above (2×10^{15} Hz and above), photons have sufficient energy to break chemical bonds (ionization), and this part of the EM spectrum is termed ionizing. The well-known human health hazards of ionizing radiation are the result of the breaking of chemical bonds in DNA. Severe damage to DNA can kill cells, resulting in tissue damage or death. Lesser damage to DNA can result in permanent changes in the cells, which may lead to mutation or cancer.

At frequencies below that of vacuum-UV light, photons do not have sufficient energy to break chemical bonds, and this part of the EM spectrum is termed nonionizing.[2] At power frequencies, for example, the photon energy is a factor of 10^{-6} smaller than that needed to break even the weakest chemical bond. Although nonionizing sources cannot break chemical bonds, there are possible mechanisms of direct interaction. Electric fields can exert direct mechanical forces on charges or cellular structures within a tissue, orient dipolar molecules, and depolarize cell membranes. Magnetic fields can also directly exert forces, but since biological materials are largely nonmagnetic, these forces are very weak. These direct effects are generally far weaker than those produced by random thermal agitation (thermal noise) and, to cause significant changes in a biological system, generally require fields that far exceed those that exist in ordinary environments (6, 7). The well-known direct hazards of electric power, shock and burns, generally require that the subject directly contact a charged surface and are outside the scope of this review.

Indirect Effects. An additional mechanism by which nonionizing EM sources, such as RF, MW, and power-frequency fields can cause biological effects is by inducing electric currents that cause heating. This heating can kill cells, and if enough cells are killed, long-term and possibly permanent tissue damage can occur. The efficiency with which a nonionizing EM source can induce electric currents, and thus produce heating, depends on the frequency of the source. At frequencies below those used for broadcast AM radio (below 5×10^5 Hz), EM sources couple poorly with the bodies of humans and animals, and thus are very inefficient at inducing electric currents and causing heating. Power-frequency magnetic fields in excess of 500 μT are needed to induce electric currents of a magnitude similar to those that occur naturally in the human body (4, 8). Well-accepted safety standards exist to protect persons from power-frequency fields that could induce such currents (4, 9).

Signal Amplification. The above considerations show that the interactions of power-frequency fields with the human body are very weak at typical environmental levels. This does not rule out the possibility of some biological effect, but special conditions would clearly be required (10). The literature abounds with speculations about how power-frequency fields might overcome signal-to-noise problems via various resonance and/or signal amplification mechanisms (11–14); however, these speculations often fail to adequately consider the issue of thermal noise, and/or are open to challenge on other technical grounds (7, 8, 15–17).

Other ELF Fields. The electric currents produced by a magnetic field are proportional to the rate of change (i.e., the time-derivative) of the magnetic field. Pulsed fields (square-wave, sawtooth, etc.) have a higher rate of change than do sinusoidal fields of the same frequency and field strength, and thus induce much higher currents. Similarly, electric currents induced in the body by alternating magnetic fields are proportional to their frequency, so that frequencies above power-frequency induce higher currents for a given field strength than do power-frequency fields.

[2] Many of the biological effects of UV, visible, and infrared frequencies are also direct effects that depend on the photon energy, but they involve electronic excitation rather than ionization and do not occur at frequencies below that of infrared light (below 3×10^{11} Hz).

Since induced electric currents are likely to be involved in any biological effect produced by power-frequency magnetic fields (4, 8), studies with pulsed and higher-frequency fields are of limited relevance to an assessment of the possible health risks associated with power-frequency fields. However, since transients and higher frequency harmonics exist in electrical environments, the biological effects of other types of ELF fields cannot be ignored. Thus, while our review of the literature on the biological effects that may be associated with the generation, transmission, distribution, and use of electricity will concentrate on studies of power-frequency sinusoidal magnetic fields, it will also consider other types of ELF fields.

Epidemiology of Power-Frequency Fields and Cancer

There have been two basic types of power-frequency epidemiology studies: studies of children (1, 18–23) (Table I) and adults (24–29) (Table II) living near distribution and/or transmission lines, and studies of adults working in occupations with presumed exposure to power-frequency fields (2, 3, 30–36) (Table III). Interpretation of these studies is greatly complicated by exposure assessment problems. If power-frequency fields were carcinogenic and were at all similar to other known carcinogens, it would be the cumulative exposure for many years prior to disease diagnosis that should correlate with cancer incidence. Unfortunately, these exposure data do not exist and cannot be reliably reconstructed.

Residential Exposure Studies. Interpretation of the residential exposure studies (Table I and II) is further complicated by the lack of consensus as to the appropriate exposure metric. The original studies that suggested a relationship between power lines and childhood leukemia used a combination of the type of wiring and the distance to the residence as a surrogate measure of exposure, a system called "wirecodes". Other studies have used distance from transmission lines or substations as surrogate measures of exposure, and some of the recent studies have used contemporary measured fields or calculated historic fields as measures of exposure. One of the most puzzling features of the residential exposure studies is that the correlation of "exposure" with cancer incidence is higher when wirecodes or calculated fields are used as an exposure metric than when fields are directly measured in the homes (19–21). In general, the various surrogate measures of exposure do not correlate well with each other, or with contemporary measured fields; none of these measures of exposure is obviously superior, and none is common to all the major studies.

There have also been a few epidemiologic studies that have examined the relationship between the use of electrical appliances and cancer (19, 20, 37–39). These studies have shown little consistent association between the use of electrical appliances and cancer incidence, although the most recent of these studies (39) has actually shown a decreased incidence of leukemia among adult users of personal appliances, a decrease which reaches statistical significance for certain subgroups.

Table I. Childhood Cancer and Residential Exposure to Power-Frequency Fields

Major studies:	Wertheimer & Leeper 1979 (1); Tomenius 1986 (18); Savitz *et al.* 1988 (19); London *et al.* 1991 (20); Feychting & Ahlbom 1993 (21); Olsen *et al.* 1993 (22); Verkasalo *et al.* 1993 (23)
Cancer sites:	Leukemia (15 studies), CNS cancer (7 studies), lymphoma (6 studies), overall cancer (4 studies)
Exposure assessment:	Contemporary measurements (4 studies), retrospective calculations (3 studies), proximity to lines (5 studies), wirecodes[a] (5 studies)
Results:	• No statistically significant associations have been found between measured fields and leukemia, brain cancer, or total cancer incidence (19–21). • One study (21) reported a statistically significant association between retrospective calculated fields and leukemia, but others (22, 23) did not. • Several studies (1, 19, 20) have reported statistically significant associations between wirecodes and brain cancer and/or leukemia incidence. • No studies have shown statistically significant associations between brain cancer and measured fields (19, 21), retrospective calculated fields (21–23), or proximity to lines (18, 21). • A statistically significant association with overall cancer incidence was reported in one study for calculated fields (22) and in one for proximity (18), but this was not observed in other studies (21, 23). • For the studies as a whole, the relative increase in cancer incidence (RR) was 1.5–1.9, but RR values as low a 1.0 (no effect) or as high as 3 cannot be excluded.
Dose-response:	• Two studies have reported statistically significant dose-response trends for leukemia and wirecodes (20) or calculated fields (21), but otherwise no statistically significant dose trends have been found.

[a] See text.

Table II. Adult Cancer and Residential Exposure to Power-Frequency Fields

Major studies:	Wertheimer & Leeper 1982 (24); McDowall 1986 (25); Coleman *et al.* 1989 (26); Youngston *et al.* 1991 (27); Schreiber *et al.* 1993 (28); Feychting & Ahlbom 1994 (29)
Major sites:	Leukemia (5 studies), CNS cancer (2 studies), total cancer (3 studies)
Exposure assessment:	Contemporary measurements (1 study), retrospective calculations (1 study), proximity to lines (4 studies), wirecodes[a] (1 study)
Results:	• A statistically significant association of brain cancer and total cancer with wirecodes was reported in one study (24), but no significant association was seen in other studies (25, 28, 29). • No statistically significant association of leukemia with exposure was found for any measure of exposure in any study (24–29). • For the studies as a whole, the relative increase in cancer incidence is about 1.1, but RR values below 1.0 (protection) or as high as 1.6 cannot be excluded.
Dose-response:	• No studies have reported statistically significant dose-response trends.

[a] See text

Table III. Adult Cancer and Occupational Exposure to Power-Frequency Fields

Major recent studies:	Floderus *et al.* 1993 (30); Sahl *et al.* 1993 (31), Guenel *et al.* 1993 (32), Theriault *et al.* 1994 (33); London *et al.* 1994 (34); Tynes *et al.* 1994 (35); Savitz & Loomis 1995 (36)
Major sites studied:	Leukemia (25+ studies), brain (18+ studies), breast (5+ studies), melanoma (5+ studies), lymphoma (5+ studies), all cancer (6+ studies)
Exposure assessment:	Early studies were based on job titles; some later studies have exposure assessment for job categories, but not for individuals.
Results:	• Some studies report an excess incidence of leukemia, brain cancer, breast cancer and/or lymphoma in some "electrical" occupations. • For leukemia, brain cancer, breast cancer and/or lymphoma, the studies as a whole show a relative increase in cancer of 1.1 to 1.2, but RR values as low as 1.0 (no effect), and as high as 1.5 cannot be excluded. • No overall cancer increase has been reported in "electrical" occupations, but RR values below 1.0 (protection) or as high as 1.1 cannot be excluded.
Dose-response:	• Only a few studies (e.g., London *et al.* [34]) have reported statistically significant dose-response relationships.

Occupational Exposure Studies. Interpretation of the occupational exposure studies (Table III) is complicated by a lack of actual dosimetry. The original studies that suggested a link between occupational exposure to power-frequency fields and cancer were based on job titles as listed on death certificates. Some of the latest studies have improved upon this by using job descriptions, supplemented by data from workers doing those jobs, to develop exposure categories. However, no studies to date have been based on direct measurements of the exposure of the actual subjects of the study. In fact, given the low incidence of the cancers implicated by the studies, it is difficult to see how any sufficiently large study could be mounted with adequate direct measurements of the subjects' exposure. Even if such personal dosimetry were available, there is no consensus as to the appropriate exposure metric, since arguments have been made for time-weighted average fields, peak fields, rate of change of fields, or even transients.

Multiple Testing Issues. Interpretation of many of the studies is further complicated by multiple testing issues. When studies include multiple exposure metrics and/or multiple types of cancer, the investigator can compare many different subgroups. Each comparison (by the commonly accepted statistical criteria) has a 5% probability of yielding a "statistically significant" difference between the groups, even if there were no real differences. A related problem arises when the investigator groups subjects into categories based on arbitrarily chosen exposure cutpoints. Were the cutpoints chosen in advance, this would not be a problem, but often multiple cutpoints are analyzed after the fact. Between multiple exposure metrics, multiple cutpoints, multiple cancer sites, and subgroup analysis, a study may contain 50 or more calculations of relative risk,[3] each individually analyzed for significance at 5%. To make matters worse, the investigator may preferentially publish the "positive" findings, raising the issue of publication bias.

In general this issue of multiple testing has not been adequately considered in analysis of the litera-

[3] The excess cancer found in epidemiological studies is usually quantified in a number called the relative risk (RR). This is the risk of an "exposed" person getting cancer divided by the risk of an "unexposed" person getting cancer. Since no one is unexposed to power-frequency fields, the comparison is actually "high exposure" versus "low exposure". A RR of 1.0 means no effect, a RR of less than 1.0 means a decreased risk in exposed groups, and a RR of greater than 1.0 means an increased risk in exposed groups.

ture on power-frequency fields and cancer, although an interesting exception can be seen in the multiple cutpoint analysis done by Olsen *et al.* (22). Publication bias is also clearly a problem, and a review by the United Kingdom National Radiation Protection Board (40) sites several specific examples.

Evaluating the Epidemiological Evidence

A specific set of criteria, first clearly enunciated by Hill (41), are widely used to assess epidemiological and laboratory studies of agents that may pose human health risks (Table IV). These "Hill's criteria" must be applied with caution. First, one must examine the entire published literature, not just pick the reports that support or contradict the existence of a health hazard. Second, one must directly review the important source documents, rather than base judgments on academic or regulatory reviews. Third, satisfying the individual criteria is not a yes-no matter, support for a criterion can be strong, moderate, weak, or nonexistent. Lastly, the criteria must be viewed as a whole; no individual criterion is either necessary or sufficient for concluding that there is a causal relationship between exposure to an agent and a disease.

How well do the epidemiological studies of power-frequency fields and cancer stand up to Hill's criteria (Table IV)? First, the association of power-frequency fields with cancer is not strong. A strong association is one with a RR of 5 or more. Tobacco smoking, for example, shows a RR for lung cancer 10–30 times that of nonsmokers. Most of the power-frequency studies that show statistically significant elevations in cancer incidence have RRs of less than three, and the studies as a whole have RRs in the 1.0 to 1.8 range (Table I–III). Second, while there are studies showing statistically significant association of cancer incidence with exposure to power-frequency fields, few studies show the same positive result, and even the positive studies are often inconsistent with each other. Many of the studies are also internally inconsistent, showing statistically significant risks for some measures of exposure, but not for others (Table I and II). Third, the specificity of the reported association of cancer with power-frequency fields is also very weak, with at least six different types of cancer being reported in excess in two or more studies. A quick overview of the residential and occupational epidemiological studies appears to indicate that exposure to power-frequency fields is associated principally with brain cancer and leukemia. However, this appearance is misleading, since in many studies leukemias and/or brain cancer are the only types of cancer evaluated. Fourth, even the studies which have reported a statistically significant excess of some type of cancer for some measure of exposure, have generally not found a statistically significant dose-response relationship (Table I–III).

Relationship of Laboratory Studies to Epidemiology in Risk Evaluation

Overall, application of Hill's criteria (Table IV) shows that the current epidemiological evidence for a connection between power-frequency fields and cancer is weak, because the existing studies are neither strong nor particularly consistent, and because there is so little evidence for a dose-response relationship. Clearly, there are at least several roles for laboratory evidence in this evaluation. First, if there were strong *in vitro* or *in vivo* evidence that power-frequencies were carcinogenic, it would make the epidemiology more convincing. Second, if there were mechanisms

Table IV. Is There a Causal Relationship Between Power-Frequency Fields and Cancer?

The classical "Hill's criteria" (41)	Hill's criteria applied to power-frequency fields and cancer	Strength of evidence[a]
Strength?	• How strong are the relative risks for an association between power-frequency fields and cancer?	Weak-possible
Consistency?	• Are the studies of associations between power-frequency fields and cancer internally and externally consistent?	Weak-possible
Specificity?	• Since many carcinogens cause multiple types of cancer, this criterion may be of limited relevance.	Weak
Temporal relationship?	• Since exposure to these fields is pervasive, this criterion is unevaluable.	—
Dose-response curve?	• Does the incidence of cancer increase with increased exposure to power-frequency fields?	None-weak
Biologically plausible and coherent?	• Are there mechanisms that could connect these fields with cancer, and that are consistent with what is known about cancer biology and about electromagnetics?	None
Experimental evidence?	• Is there laboratory evidence that these fields are carcinogenic?	None-weak
Overall	• How strong is the evidence for a causal relationship between power-frequency fields and cancer?	Weak

[a] On a 5-point scale of how well the data as a whole support as causal relationship between exposure to power-frequency fields and an increased risk of cancer: none, weak, possible, probable, strong.

that could explain an interaction of power-frequency fields of the intensity encountered in residential and occupational settings with biological systems, then many of the questions concerning the appropriateness of various exposure metrics could be resolved. On the other hand, if appropriate laboratory studies were done and these studies consistently failed to show any evidence for carcinogenicity, then we would tend to dismiss this weak and inconsistent epidemiology. In other words, while weak epidemiology cannot establish causality on its own, weak epidemiology combined with strong laboratory evidence and plausible mechanisms can satisfy the criteria for causality.

Bioeffects of Intense Fields. Power-frequency fields intense enough to induce electric currents in excess of those that occur naturally (above 500 μT) have shown reproducible effects, including effects on humans (4, 9, 42, 43). However, these "bioeffects" have no obvious connection to carcinogenesis and have not been observed at the field intensities encountered in occupational and residential settings.

Genotoxicity. If power-frequency fields were carcinogenic, they could be either genotoxic or epigenetic (in older terminology, either initiators or promoters). Genotoxic agents directly damage the genetic material of cells (the DNA), often affect many types of cells, and may cause more than one kind of cancer. Genotoxins may not have thresholds for their effect; in other words, as the dose of the genotoxin is lowered the risk gets smaller, but it may never go away.

Epigenetic Activity. An epigenetic agent, on the other hand, is something that increases the probability that a genotoxin will damage the genetic material of cells, or that a genotoxic exposure will result in cancer. Promoters are a particular kind of epigenetic agent that increase the cancer risk in animals already exposed to a genotoxic carcinogen. Epigenetic agents (including promoters) usually affect only certain types of cells and may cause only certain types of cancer. Epigenetic agents generally have thresholds for their effect, so that as the dose of an epigenetic agent is lowered a level is reached at which there is no (rather than very little) risk.

Power-Frequency Fields and Genotoxicity

There are many approaches to measuring genotoxicity. Whole-organism exposure studies can be used to see whether exposure causes cancer or mutations. Cellular studies can be done to detect DNA or chromosomal damage. The genotoxicity studies done to date are summarized in Table V. This summary includes nonmammalian as well as mammalian data, and includes both pulsed fields and ELF fields at other than power-frequency. Such broad coverage is warranted, since any evidence for genotoxicity from any system exposed to any related type of field would be relevant to the question of carcinogenicity.

Whole Organism Genotoxicity. The biggest gap in the range of endpoints assessed is that very few mammalian exposure studies have been published (see Loscher & Mevissen [44] for summaries of some of the unpublished work). Bellossi *et al.* (45) exposed leuke-

Table V. Assessment of the Genotoxicity of Power-Frequency Fields[a]

Endpoint	Results
Carcinogenesis	• Sinusoidal fields not a carcinogen in mice (46). • Pulsed 12- and 460-Hz fields not leukemogenic in mice (45).
Mutagenesis	• Sinusoidal fields not mutagenic in mice (47), Drosophila (126), yeast (62), mammalian cells (63), or bacteria (61, 63). • Pulsed fields not mutagenic in bacteria (60).
Chromosome aberrations (occupational-exposure)	• No excess sister chromatid exchanges (SCEs) (67–70). • Excess chromosome aberrations in smokers only (69, 70). • Excess chromosome aberrations in non-smokers in one study (67), but not in other studies (68–70).
Chromosome aberrations (*in vitro*)	• Sinusoidal fields do not cause chromosome aberrations in human lymphocytes[b] (53, 54). • Sinusoidal fields do not cause SCEs in human[b] (54–56) or rat lymphocytes (57). • Pulsed fields caused aberrations in human lymphocytes in one study (65), but not in a replicate (59) or in CHO cells (66).
DNA strand breaks	• Sinusoidal fields do not cause DNA strand breaks in human cells[b] (49), CHO cells[b] (48), or plasmids (50). • Pulsed fields do not cause DNA strand breaks in human cells[b] (52).
Cell transformation	• No increase in transformation of mammalian cells (64).
Micronucleus formation	• Neither sinusoidal[b] (56, 58) nor pulsed (59) fields increase micronuclei formation in mammalian cells.

[a] Studies are of 50/60 Hz magnetic fields unless otherwise specified.
[b] Electric fields and combined electric and magnetic fields were also tested.

mia-prone mice for five generations and found no effect on leukemia rates; however, since the study used 12 and 460 Hz pulsed fields at 6000 μT, the relevance of this to environmental power-frequency fields is unclear. Rannug *et al.* (46) found that 50 and 500 μT fields at 50-Hz did not significantly increase the incidence of skin tumors or leukemia in mice. In a multigeneration mouse exposure study which used 300 μT (plus 15 kV/m) or 1000 μT (plus 50 kV/m) 60-Hz fields, Benz *et al.* (47) found no increase in mutation rates, fertility, or sister chromatid exchanges.

Cellular Genotoxicity. Cellular genotoxicity studies have been much more extensive (Table V); the most obvious gap is the lack of studies using cell transformation endpoints. Published laboratory studies have reported that power-frequency magnetic fields do not cause DNA strand breaks (48–52), chromosome aberrations (53, 54), sister chromatid exchanges (SCEs) (54–57), micronuclei formation (56, 58, 59), or mutations (60–63), and do not transform cells (64). Many of these laboratory studies also examined power-frequency electric fields and combinations of power-frequency electric and magnetic fields, and as with the studies of magnetic fields alone, the studies of electric fields and combined fields showed no evidence of genotoxicity.

Positive Reports of Genotoxicity. There are two published reports of genotoxicity. Khalil and Qassem (65) reported that a 1050 μT pulsed field caused chromosome aberrations, but Scarfi *et al.* (59) were unable to replicate this observation, and Takahashi *et al.* (66) found no effect in similar studies with CHO cells. Nordenson *et al.* (67) reported that switchyard workers exposed to spark discharges[4] had increased chromosomal defects, but Bauchinger *et al.* (68) found no such increase in a similar study. Two other studies (69, 70) found some evidence of increased chromosomal aberrations in workers exposed to spark discharges, but only if they were also smokers.

Summary of Genotoxicity. The evidence is quite convincing that power-frequency fields are not genotoxic. Only the lack of cell transformation and long-term animal exposure studies keeps the data from being totally convincing. This conclusion is supported by two recent comprehensive reviews on this subject. McCann *et al.* (71) wrote, "The preponderance of evidence suggests that neither ELF nor static electric and magnetic fields have a clearly demonstrated potential to cause genotoxic effects," and Murphy *et al.* (72) wrote, "Considering the total body of available information, there is little evidence that exposure to [power-frequency fields] directly causes genetic changes in biological systems."

Power-Frequency Fields and Epigenetic Activity

Even before the evidence accumulated that power-frequency fields were not genotoxic, some investigators suggested that these fields were promoters. As a result, extensive investigations have been conducted of the possible epigenetic activity of power-frequency fields. These studies are summarized in Table VI.

Classical Promotion Assays. Promoters are a specific class of epigenetic agents. In a classical promotion test, animals are exposed to a known genotoxin at a dose that will cause cancer in some, but not all, animals. Another set of animals are exposed to the genotoxin, plus another agent. If the agent plus the genotoxin results in more cancers than are seen for the genotoxin alone, then that agent is a promoter. Copromotion is a related assay in which the agent is tested with both a known genotoxin and a known promoter.

Published studies have reported that power-frequency magnetic fields do not promote chemically induced skin (46, 73–75) or liver cancers (76, 77). For chemically induced breast cancer, published studies have reported promotion at 20 μT (78) and 100 μT (79), but other studies did not find promotion at 0.3–1.0 μT (80), 100 μT (81), or 30,000 μT (82). The report by Beniashvili *et al.* (78) of promotion of chemically induced breast cancer at 20 μT is difficult to evaluate, as the study has been published only in preliminary form, and critical experimental details are missing.

Cellular Epigenetic Activity. Some types of studies are relevant to the carcinogenic potential of agents, but are neither classic genotoxicity nor promotion tests. The most common of these are cellular studies that test whether an agent enhances the activity of a known genotoxin; these studies could be regarded as the cellular equivalent of a promotion study. Published studies have reported that power-frequency magnetic fields do not enhance the mutagenic effects of known genotoxins (61, 63) and do not inhibit the repair of DNA damage induced by ionizing (83) or UV (62) radiation.

Positive Reports of Epigenetic Activity. In addition to the two reports of promotion of chemically induced breast cancer (78, 79), three studies have indicated that power-frequency fields might have some epigenetic activity. Rosenthal *et al.* (54) reported that a 5,000 μT power-frequency field might increase the frequency of SCEs induced in lymphocytes by antineoplastic drugs; and Hintenlang *et al.* (84) reported that 600–1,500 μT power-frequency fields increased the frequency of tetraploidy in lymphocytes when combined with high doses of ionizing radiation. Neither study has been replicated. Cain *et al.* (64) re-

[4] Spark discharges are unique to the electrical environment of high-voltage sources, where electric fields can reach intensities of up to 20 kV/m. The peak value of the body current at the point of a spark discharge can reach several amps (67).

Table VI. Assessment of the Epigenetic Potential of Power-Frequency Fields[a]

Endpoint	Results
Promotion (chemically induced skin tumors)	• No promotion or co-promotion at 2000 μT (73, 74). • No promotion at 50 or 500 μT delivered continuously (46, 75) or intermittently (75)
Promotion (chemically induced mammary tumors)	• Promotion at 20 μT (78) and 100 μT (79). • No promotion at 0.3–1.0 μT (80), 100 μT (81), or 30,000 μT (82).
Promotion (chemically induced liver tumors)	• No promotion at 0.5–500 μT (76). • No co-promotion at 0.5 or 500 μT (77).
Inhibition of DNA repair	• No effect on UV-induced DNA damage in yeast at 1000 μT (62). • No effect on radiation-induced DNA damage in human lymphocytes at 1000 μT (83).
Enhancement of transformation	• Enhanced co-transformation of mammalian cells at 100 μT (64) in some, but not all experiments.[b]
Enhancement of genotoxicity	• Enhancement of ionizing radiation damage in human lymphocytes at 600 μT (84). • Enhancement of chemically-induced sister chromatid exchanges in human lymphocytes at 5000 μT for some, but not all agents (54). • No enhancement of chemical mutagenesis in bacteria at 0.12–120 μT (61). • No enhancement of viral-induced mutagenesis in human cells at 1 or 10 μT (63).

[a] All studies are of 50/60 Hz sinusoidal magnetic fields.
[b] See text and Footnote 5.

ported that a 100 μT power-frequency field could enhance cell transformation; the effect was only seen in the presence of a chemical promoter, and the authors subsequently reported[5] that they could not replicate the study.

Summary of Epigenetic Activity. In general, power-frequency fields do not appear to have epigenetic activity. However, there are areas that need further exploration. The reports of promotion of chemically induced breast cancer (78, 79) and enhancement of genotoxicity (54, 84) need to be replicated, and if they are replicated the dose-response relationship for the effect needs to be established.

Bioeffects of Power-Frequency Fields That Might Be Related to Cancer

Biological effects other than genotoxicity, promotion, or enhancement of genotoxicity might be related to cancer. In particular, agents that have dramatic effects on cell growth (mitogenic effects), on the function of the immune system, or on hormone balances, might contribute to cancer without meeting the classic definitions for genotoxicity, promotion, or epigenetic activity. Studies of these issues are summarized in Table VII.

Cell and Tumor Growth. There have been scattered reports that power-frequency fields can enhance cell proliferation (54) or tumor growth (74, 79, 81), but the few positive reports have involved fields of 100 μT and above, and the vast majority of the studies* have shown no effect. Two other studies have been cited to support the idea that power-frequency fields might be mitogens. Liboff *et al.* (92) are often quoted as reporting effects on cell growth for fields as low as 16 μT, but the study only reports increased uptake of a DNA precursor, an observation which may or may not indicate an effect on proliferation. Phillips *et al.* (93) reported enhanced growth of tumor cells at 100 μT, but the statistical significance of the effect has been questioned, and the study could not be replicated (94).

Immunosuppression. In the early 1970s, some investigators speculated that the immune system might have a role in preventing the development of cancer, a theory known as the "immune surveillance hypothesis" (95, 96). Subsequent studies have shown that this hypothesis is not generally valid (95, 96). Suppression of the immune system is associated with increased rates of certain types of cancer, particularly lymphomas, but not with leukemia or brain cancer (95, 96). While some studies have reported that power-frequency fields can have effects on cells of the immune system (97), no studies have shown the type or magnitude of immune suppression that is associated with an increased incidence of lymphomas or other cancers in humans or animals.

[5] Cain CD, Thomas DL, Adey WR. 60-Hz magnetic field strength dependency and TPA-induced focus formation in co-culture of C3H/10T1/2 cells. Abstract P-1, Annual Review of Research on Biological Effects of Electric and Magnetic Fields from the Generation, Delivery and Use of Electricity, Albuquerque, November 1994.

* References 46, 49, 53, 55–57, 73, 75–77, 80, 82, 85–91.

Table VII. Assessment of Biological Effects That Might Be Related to Carcinogenesis[a]

Endpoint	Results
Effects on tumor growth	• Enhanced growth of chemically induced skin tumors at 2000 μT in one study (74), but not in another (73), and not at 50 or 500 μT (46, 75). • Enhanced growth of chemically-induced mammary tumors at 100 μT (79, 81), but not at 0.3–1.0 μT (80) or 30,000 μT (82). • No growth effect on mammary tumors at 100–2000 μT[b] (88), on liver tumors at 0.5–500 μT (76, 77), or on leukemia at 1.4–500 μT (87).
Effects on cell growth	• Increased proliferation in human lymphocytes at 5000 μT (54). • No effect on growth of mammalian cells at 220–30,000 μT (56, 57, 86, 89). • No effect on growth of human lymphocytes at 100–220 μT[b] (53, 55, 56). • No effect on growth of human tumor cells at 0.2–2500 μT[b] (49, 85, 90, 91).
Growth-related effects	• Increased thymidine uptake in human fibroblasts at 16+ μT (92). • Increased colony-forming ability of tumor cells at 100 μT[c] (93).
Immune suppression	• Scattered reports of minor effects on components of the immune system at 2000 μT and above, but no evidence of immune-suppression (97).
Altered hormone balance	• Decreased night-time melatonin in rats at 1–50 μT (100), 0.2–1.0 μT (103), and at 0.3–1.0 μT (80), but not at 0.10 μT (100) or 1 μT (102). • Inconsistent effect on melatonin in Siberian hamsters at 100 μT (104). • Reports of decreased night-time melatonin levels due to exposure to sinusoidal electric fields and static magnetic fields (98, 127). • No effect on melatonin levels in sheep at 4 μT (101). • No evidence that melatonin has significant anti-cancer activity in humans (106, 107).

[a] All studies are of 50/60 Hz sinusoidal magnetic fields unless otherwise noted.
[b] Electric fields and combined electric and magnetic fields also tested.
[c] Attempt at replication failed (94).

The "Melatonin Hypothesis". Some investigators have suggested that power-frequency fields might suppress the production of melatonin, and that melatonin might have "cancer-preventive" activity (98, 99). This is highly speculative. There have been reports that electric fields and static magnetic fields can affect melatonin production (98), but studies using power-frequency magnetic fields have not shown consistent effects (80, 100–104). The second component of the hypothesis, that a decrease in melatonin levels will lead to an increase in cancer, is also unproven. In the late 1970s and early 1980s there was interest in using melatonin as an anti-cancer agent (105), but clinical trials of melatonin continue to show that it is largely ineffective (106, 107).

Reproducibility and Replication. If a reproducible biological effect is defined as one that has been reported in the peer-reviewed literature by more than one laboratory, without contradictory reports appearing elsewhere; then there may be no reproducible effects of ELF magnetic fields below about 200 μT. While there are reports of effects for fields as low as about 1 μT, none of these reports have been replicated.

The lack of confirmation of the laboratory studies is due to many factors. First, many reports on the biological effects of power-frequency fields have never been published in the peer-reviewed literature and cannot be scientifically evaluated. Second, no attempts have ever been made to replicate many of the published reports of biological effects; and one positive report, standing in isolation, is hard to evaluate. Third, when attempts have been made to replicate some of the published studies, these replications have often failed to show the effect (89, 108, 109). Lastly, the investigators in this field use a wide variety of biological systems, endpoints, and exposure conditions, which makes studies extremely hard to compare or evaluate. A recent review (110) concluded:

> Despite earlier reports of the effects in a diverse range of models there has not been a single positive replication of any study during 1993, instead the range of unreplicated studies has continued to grow. The few replications that have been attempted have all failed to confirm the original findings.

Mechanisms for Biological Interactions

Three general biophysical mechanisms have been proposed that could account for biological effects of strong ELF magnetic fields. Biological effects could be due to induced electric currents (4, 8, 9), to direct effects on magnetic biological material (12), or to effects on rates of certain chemical reactions (111). However, when quantitatively analyzed all these

mechanisms are found to require fields in tissue that far exceed the fields that are induced by typical environmental exposures.

Induced Currents. Power-frequency magnetic fields can induce electric currents, and induced electric currents definitely can cause biological effects (4, 8, 9). However, the currents induced in the body by fields of less than 50 μT are weaker than the currents that occur naturally (8). Moreover, the currents induced by a 5 μT power-frequency field are less than those induced in the body by walking through the Earth's static magnetic field (8). Thus, as emphatically pointed out by Adair (7, 8), if power-frequency magnetic fields of the intensity encountered in residential and most occupational settings do have biological effects, they are not mediated by induced electric currents.

The above argument presumes that 50 or 60 Hz sinusoidal power-frequency fields are the only time-varying electromagnetic fields found in conjunction with the transmission, distribution, and use of electric power. If this presumption is not true, and large transients and/or significant higher-order harmonics are present, then it is possible that electric currents stronger than those that occur naturally in the body could be induced at field levels that are present in residential and occupational settings.

Magnetic Biological Material. Small magnetic particles (magnetite, Fe_3O_4) have been found in bacteria that orient in the Earth's static magnetic field (12). While investigators (12) have speculated that such magnetic particles may also exist in fish, honeybees, and birds, their presence in mammalian cells is still unproven, and their biological function in mammalian tissue is unknown. Kirschvink *et al.* (12) have suggested that power-frequency magnetic fields could cause biological effects by acting directly on such particles. However, calculations show that this would require fields of 2–5 μT or above at 50/60 Hz (7, 12, 112).

Free Radical Reactions. *Static magnetic fields* can influence the reaction rates of chemical reactions that involve free radical pairs (111, 113). Since the free radicals involved in these reactions have lifetimes in the microsecond range, whereas power-frequency fields have a cycle time in the millisecond range, a power-frequency field will act like a static field during the time scale over which these reactions occur. However, since any effects of the power-frequency field would be additive with the Earth's static field (30–70 μT), no detectable biological effects would be expected below about 50 μT (111).

Resonance Theories. Some of the biophysical constraints on possible mechanisms for biological effects of weak power-frequency magnetic fields could be overcome if there were resonance mechanisms that could make cells (or organisms) uniquely sensitive to power-frequency fields. Several such resonance mechanisms have been proposed, but none have survived scientific scrutiny (8, 15–17), and much of the experimental evidence that prompted the speculations in the first place cannot be independently reproduced (89, 108, 109). There are also severe incompatibilities between known biophysical characteristics of cells and the conditions required for such resonances (8, 15–17).

Summary. None of the above mechanisms appear to be able to explain the existence of biological interactions at field levels that are present in residential and occupational settings. Thus, if power-frequency fields below 5 μT do actually have biological effects, the mechanisms must be found, in Adair's (8) words, "outside the scope of conventional physics."

How Strong Is the Evidence?

Hill's Criteria. As discussed earlier, a review of the epidemiological evidence shows that the association between exposure to power-frequency fields and cancer is weak, inconsistent, and nonspecific. The laboratory studies of power-frequency fields show little evidence of the type of effects on cells or animals that point towards power-frequency fields causing or contributing to cancer. Finally, from what is known about the biophysics of power-frequency fields, and about the effects of power-frequency fields on biological systems, there is no reason even to suspect that they would cause or contribute to cancer.

A formal evaluation of the evidence using Hill's criteria (Table IV) indicates that the evidence for an association between power-frequency fields and cancer is weak. Other reviewers who have formally used Hill's criteria to evaluate the data have given overall evaluations ranging from "at best weak" evidence (114, 115) to "possible" evidence (116, 117).

Independent Review. A number of independent bodies have reviewed the research on power-frequency fields over the past several years. Of particular note are reviews by the Public Utility Commission of Texas (118), the Connecticut Academy of Science and Engineering (119), Oak Ridge Associated Universities (commissioned by the U.S. Committee on Interagency Radiation Research and Policy Coordination) (120), the United Kingdom National Radiological Protection Board (4, 121), the French National Institute of Health and Medical Research (INSERM) (122), and the French Academy of Medicine (123). None of these reviews have concluded that power-frequency magnetic or electric fields of the intensity encountered in residential, or in most occupational, settings are confirmed human health risks.

Standards and Guidelines. A number of governmental and professional organizations have developed exposure standards for power-frequency fields. Most

generally applicable are those developed by the British National Radiation Protection Board (NRPB) (4), and the International Commission on Non-Ionizing Radiation Protection (ICNIRP)[6] (9). These standards are based on keeping the electric currents induced by power-frequency fields to a level less than those that occur naturally in the body. The NRPB guidelines (4) for residential and occupational exposure to 60-Hz fields are 10 kV/m for the electric field and 1330 μT for the magnetic field (at 50-Hz the standards are 12 kV/m and 1600 μT). For the general public, the ICNIRP magnetic field exposure standard (9) is 100 μT for continuous exposure and 1000 μT for short-term exposure. For occupational exposure, the ICNIRP standard is 500 μT for continuous exposure and 5000 μT for short-term exposure.

Consensus. There is, then, a broad consensus in the scientific community that no causal association has been established between residential and occupational exposure to power-frequency fields, and the risk of cancer. There is also a broad consensus that exposure to these fields has not been, and probably cannot be, proven to be absolutely safe. The controversy in the scientific community is over whether power-frequency fields might be shown to be hazardous by future studies, and the related issue of what additional studies should be done, and what priority should be given to those studies.

What Additional Studies Are Needed?

No number and type of additional studies will be sufficient to satisfy those who demand total assurance that there are absolutely no health effects. Given the ambiguities of risk research and the nature of the scientific method, there will always be loose ends and unexplained findings. Nevertheless, there appear to be certain areas where additional studies might be useful.

Epidemiology. Large studies, with individual dose assessment, control of known confounders, and the capability of examining dose-response relationships would have a major impact on risk assessment. Individual dose assessment, however, would appear to require prospective studies, and it is not clear that any such studies are planned or even feasible. It is difficult to see how more retrospective occupational and residential exposure studies will resolve anything, particularly if they are based on surrogate measures of exposure. However, there are areas where small epidemiological studies might have a great impact. If, for example, a confounder were identified in the childhood leukemia-wirecoding studies (see for example, Jones *et al.* [124]), or a carcinogen was identified in some "electrical occupations," almost all basis for concern about power-frequency fields and cancer would vanish.

Animal. An obvious gap in the genotoxicity studies is the relative lack of long-term animal exposure studies. Such studies are underway in the United States and elsewhere. A positive finding of carcinogenicity in these studies, particularly if it was for leukemia or CNS cancer, would require a major reevaluation of the public health implications of occupational and residential exposure to power-frequency fields. However, a negative outcome would have little impact. First, almost no one expects that power-frequency fields will be found to be genotoxic. Second, proponents of the idea that these fields do cause cancer could simply claim that the exposures were done under the wrong conditions.

In addition to long-term exposure studies, the two positive reports of promotion of chemically induced breast cancer (78, 79) need to be replicated, and if they are replicated the dose-response relationship for the effect needs to be established. Promotion studies of leukemia and CNS cancer would also be valuable, but there are no established promotion models for either type of cancer.

Cellular. An obvious gap in the cellular genotoxicity studies is the relative lack of cellular transformation assays. Without getting into the argument about whether transformation measures genotoxicity or epigenetic activity, clearly either positive or negative finding of enhancement of transformation would influence thinking. There are also two isolated reports of enhancement of genotoxicity (54, 84) that need to be replicated, and if they are replicated the dose-response relationship for the effect needs to be established.

The Public Controversy About "EMF and Cancer"

Regardless of the scientific review of the data, the public controversy remains. This is seen in the continuing litigation over cancers that have been alleged to be caused by occupational and residential exposures, and by the public opposition that meets almost all attempts to site new powerlines and substations or to upgrade existing facilities. The public concern is sustained by the occasional reports of positive findings, by the inability of scientists to guarantee that no risk exists, and by statements from scientists and government officials that more research is needed. This public concern is further encouraged by several lay-oriented books that allege that there has been a conspiracy to conceal the health risks of power-frequency fields from the general public (125). Concern has also been nourished by uneven reporting on this issue by the mass media. For example, the 1993 report from

[6] The 1990 "interim standard" was confirmed by the ICNIPR in a press release dated May 12, 1993.

Sweden (21) of a positive association between calculated historic fields and childhood leukemia received wide media coverage in the United States, but the parallel negative reports from Denmark (22) and Finland (23) received little or no mention, and the recent Swedish study (29) showing no association between adult residential exposure and cancer received essentially no coverage.

Public concern about electricity and cancer will continue either until future research shows that the fields are hazardous (an outcome we personally consider unlikely), or until the public learns that science cannot provide absolute guarantees that anything is absolutely safe (an outcome, unfortunately, that we consider equally unlikely).

This review draws heavily on an electronic FAQ (Frequency Asked Questions) document called "Powerlines & Cancer FAQs" which J. Moulder maintains in the USENET newsgroup called "sci.med.physics". We would like to acknowledge the many readers of sci.med.physics who have contributed suggestions, comments, and corrections to the FAQ sheet. The current version of "Powerlines & Cancer FAQs" can be found on USENET or obtained by FTP, e-mail, Gopher, or World Wide Web from any of the many sites that archive USENET FAQ sheets.

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