EMF
AND CHILDHOOD LEUKEMIA

by Robert Syfers

PHOTO BY ROB KAVET

The Story in Brief

Decades of research have studied possible health effects of exposure to electric and magnetic fields. While the great majority of studies have shown no link between EMF and a variety of maladies, several key epidemiologic studies have caused expert scientific panels to conclude that there is indeed a statistically significant association between power-frequency magnetic fields and the development of childhood leukemia. Nevertheless, laboratory confirmation and a convincing explanation of the nature of this link have eluded researchers and health theorists for some years. EPRI is now addressing two theories that may finally clarify the issue.

Researchers have been studying the possible health effects of exposure to electric and magnetic fields (EMF) since the late 1960s, and EPRI has been a significant part of this worldwide effort since the Institute was founded, in 1973. The early period of EMF study, which extended through the mid-1980s, focused primarily on electric fields, with little to no attention paid to cancer as a health outcome of potential concern. No scientific evidence emerged from that period that would link electric field exposure to adverse health effects in people.

About 20 years ago, the emphasis switched dramatically to the potential relationship between magnetic fields in homes and childhood cancers—particularly leukemia and brain cancer. Soon thereafter, researchers as well as state and federal agencies expanded this concern to cover occupational exposures and a far wider variety of health endpoints, including miscarriage, adult cancers of various types, cardiovascular diseases, and neurodegenerative illnesses such as Alzheimer's and amyotrophic lateral sclerosis (Lou Gehrig's disease). With its members' support, EPRI assumed a major role in this widening effort as well, addressing questions of potential health risk and developing measurement and software tools for researchers.

After a period of intense worldwide study through the 1990s, several national and international expert panels convened to evaluate the possible risks posed by EMF environments. Collectively, these deliberations narrowed concern from the broad array of health endpoints that had been studied to only one—childhood leukemia. When the results of many epidemiologic studies (studies that explore the patterns of disease and health in human populations) were evaluated and blended into a single analysis, a moderate association between magnetic fields above 3–4 milligauss (mG) and the occurrence of childhood leukemia—up to a doubling of risk—was evident. Because positive associations originated from studies of different designs from different countries, each with its own unique electrical transport system, random chance as a basis for this association was believed to be extremely unlikely.

From a scientific perspective, however, the presence of an epidemiologic association does not, by itself, constitute or substantiate a cause-and-effect relationship, which generally requires supporting results from the laboratory and a plausible mechanism of interaction. Indeed, laboratory studies using animals and cells have not supported a link between magnetic field exposures and childhood leukemia, and scientists have not identified a biophysical mechanism by which the low-level fields measured in homes could plausibly interact with biological tissue. Though random chance has been virtually ruled out, the possibility remains that the study results are somehow skewed or that another, unidentified exposure is involved. EPRI's EMF health assessment program is working to uncover a rational basis for the unexplained relationship between magnetic fields and childhood leukemia.

Over the past seven years, EPRI scientists have shifted the search into high gear, exploring two viable hypotheses, each of which may contribute to the ultimate explanation. One addresses the possibility, as suggested by many epidemiologists in the EMF community, that the link between magnetic fields and childhood leukemia is a product of artifact in study design—that in fact there is no causal basis at all; the prime suspect behind this possibility is a problem known as selection bias. The second hypothesis explores the possibility that an unrecognized exposure, contact current, is the active agent that has operated behind the scene, with magnetic fields at center stage.

Selection Bias

The term *bias* does not imply willful action by the investigator, but rather results from an undetected factor that insinuates itself into a study's execution and unintentionally skews the results. The selection bias hypothesis is based on the fact that the epidemiologic studies in question are virtually all of case-control design; for studies of rare diseases like leukemia, this design is the most practical option.

In a typical EMF case-control study, the distribution of magnetic field exposure across a group of children with leukemia is compared with the exposure distribution of children who are leukemia-free. The children with leukemia are referred to as cases, and those who are disease-free, as controls. The control group serves as a reference intended, in the ideal, to reflect the actual distribution of exposure through the greater population from which the cases originated. Thus if after carefully collecting and analyzing all of a study's data, an epidemiologist were to observe that exposure to an environmental influence was much more common in a set of cases than in a valid set of controls, that observation would suggest that the exposure under study represented a legitimate risk factor. However, the key word above is *valid,* for even if all else is done correctly and meticulously, if the controls are unrepresentative, the study results will be viewed in a dimmer light as possibly skewed by selection bias.

How could selection bias invalidate a result in concept? First, epidemiologists are generally able to identify all, or almost all, of the cases of the disease of interest within a study region—say, a metro area, a state, or a group of states. This is especially true of cancer cases, which are logged into registries that are available for public health surveillance, as well as for research purposes. The problem of selection bias usually concerns the selection and recruitment of controls—hence the expanded term *control selection bias.* If, because of selection pressures, the control group actually enrolled either under- or overrepresents the exposure of interest, then the study results will report risks that are artificially high or low, respectively.

As an example, consider the repeated observation that fewer people from lower socioeconomic groups participate in epidemiologic studies than people in higher socioeconomic strata. Further consider

that people in lower strata tend to reside in less desirable neighborhoods—frequently near freeways and very possibly adjacent to transmission or distribution corridors, where magnetic field exposures would be relatively greater than in areas typical for other segments of the population. In the event that potential control subjects from these lower socioeconomic neighborhoods are underrepresented in a study of magnetic fields and childhood leukemia—because of refusal, unavailability, or simply indifference—then their relative absence will skew downward the exposure distribution of the control subjects that are enrolled. In other words, higher magnetic field exposures will falsely appear to be rarer in the background population than in the cases, leading to the suggestion that the magnetic field is a risk factor, when in fact the result is driven by control selection bias.

In 2001, the EMF health assessment program launched a full-scale foray into the question of control selection bias with a workshop in Canada, in which EPRI scientists gathered with an international group of eminent epidemiologists to brainstorm the best ideas to guide the program's research. Under the leadership of Gabor Mezei of the EPRI program, the research has been gathering full momentum, with several reports already published in the scientific literature and new studies coming on board. Many of these address the question of selection bias caused by differential participation across socioeconomic strata, as described above. The jury remains out with respect to the extent that control selection bias may have influenced earlier studies.

Contact Current

Contact current is current that flows within a person when two locations on that person's body are in contact with electrically conductive surfaces at different electrical potentials, or voltages. For example, if the thumb and forefinger are in contact with the top and bottom of an ordinary AA battery, a small current will flow in the loop created by the fingers and the battery. If the fingers are dry, the current will be relatively small, as dry skin has a high electrical resistance; with wet fingers, the moisture will breach the skin's insulation, lowering its resistance so that comparatively more current will flow. Likewise, contact current can travel through portions of the body from one hand to the other or to a foot, should those extremities be in contact with surfaces of different voltages.

The issue of contact current safety goes back to well before the EPRI program became involved with this exposure in terms of the EMF health issue. Underwriters Laboratories specifies limits for leakage currents from home appliances of 0.5–0.75 milliampere (mA), depending on the device; the National Electrical Safety Code limits exposure to 5 mA in the rights-of-way of high-voltage overhead transmission lines; and guideline-setting bodies, such as the International Commission on Non-Ionizing Radiation Protection and the Institute for Electrical and Electronic Engineers, recommend contact current limits of anywhere between 0.5 and 1.5 mA, depending on exposure circumstances. All of these limits are intended to reduce the chance of annoying or even hazardous startle or pain reactions to the exposure. EPRI's EMF research deals with lower exposure levels, which fall below the threshold of sensory perception.

Since 1999, Robert Kavet, program manager for EMF health assessment, has led EPRI's research on contact current as a factor that could explain the association of magnetic fields with childhood leukemia. Actually, the idea of a possible role for contact current in EMF health studies occurred to Kavet in the late 1990s, after the publication of several studies suggesting that one's occupation as a seamstress or tailor was a risk factor for neurodegenerative disease; the studies' authors attributed their results to magnetic field exposure from sewing machines. Kavet visualized the machine operators' manual contact with the machines through an entire workday, and with a quick back-of-the-envelope calculation, he realized that the dose of electricity in the body from contact current, particularly in the extremities, would dwarf the doses associated with magnetic fields from the machines. This line of research led to the development of a personal meter to measure occupational exposures to contact current; the meter was put to work in an EPRI study that reported that occupational exposures to contact current would be more likely to occur when equipment was poorly grounded. At about the time Kavet was considering occupational scenarios, thought was given also to the possibility of residential contact current exposures in children vis-à-vis the childhood leukemia connection with magnetic fields.

How would a child be exposed to contact current in a residence? The most likely exposure, according to EPRI's research, results from grounding practices intended to provide electrical safety and fire protection. In the United States, the National Electrical Code has since 1918 required that a residence's electrical service be grounded to an available metal (electrically conductive) water pipe within the residence. As a result of this grounding connection, a small neutral-to-earth voltage—usually less than 1 volt—will appear on the water pipe, arising from household currents returning via the water pipe back to the substation or from induction on the neutral system from nearby sources of magnetic fields, such as overhead transmission lines or heavily loaded distribution primaries. This voltage will extend across all contiguous elements of the water system, including the metal water fixtures in a bathtub, sink, or shower. If the drainpipe sunk into the earth under a bathtub, sink, or shower is also made of metal, a bathing child touching the faucet or water stream will receive a contact current into the arm and through the body; in all but very extreme cases (for example, cases where there is a broken ground connection), these exposures are imperceptible, even to a small child. The current pathway includes the bone marrow (the site of leukemia development), with the highest dose

A Short History of EMF Research

by Rob Kavet

Questions about possible health effects from exposure to power-frequency electric and magnetic fields (EMF) in the United States first arose in the late 1960s and early 1970s, following the introduction of extra-high-voltage (765-kV) overhead transmission. The founding of EPRI in 1973 provided the U.S. electric power industry with an ideal organizational structure for investigating concerns about EMF health questions. For over a decade, EPRI's EMF research agenda, coordinated with a U.S. Department of Energy (DOE) EMF research program, focused mainly on electric fields.

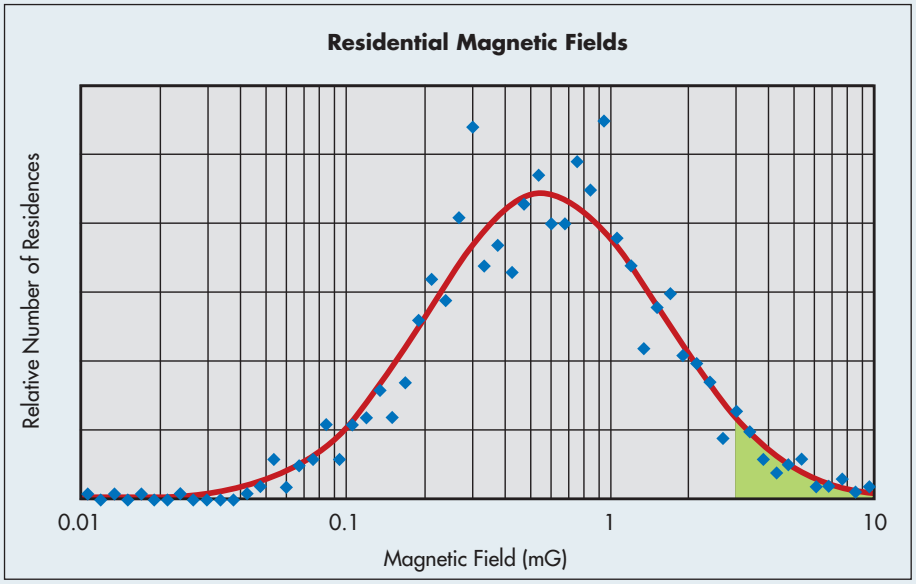
Two noteworthy studies played a major role in redefining the EMF research agenda. The first study, published in 1979 by Wertheimer and Leeper, reported an association between residential proximity to heavily loaded distribution lines and childhood cancer mortality (including mortality from leukemia) in the Denver metropolitan region. In this study, exposure within a residence was assessed using so-called wire codes based on visual aspects of lines, such as line type (for example, one-, two-, and three-phase primaries and secondaries) and wire thickness (a crude index of line loading), and their distance from the residence. This scheme for exposure characterization became known as the Wertheimer-Leeper wire code. The authors' suggestion that magnetic fields could be responsible for the reported association could be neither substantiated nor refuted.

In 1988, a team headed by David Savitz published a second study. The Savitz study differed from the Wertheimer and Leeper study in its use of a more recent set of childhood cancers and a study design that included actual residential measurements of magnetic (and electric) fields as well as wire codes. Also, in accordance with accepted contemporary practice, the Savitz study analyzed cancer incidence (new diagnoses) rather than mortality statistics, which had been used in the earlier study. Once again, associations were seen between wire codes and childhood cancers. In addition, the study showed that homes with higher wire codes had higher measured magnetic fields, although, interestingly, the association with cancer reported for the measured fields was weaker than the association based on wire codes.

Publication of the Savitz study marked a permanent change in the focus of EMF research. By this time, a large body of research supported by both DOE and EPRI had failed to uncover any acute hazard associated with electric field exposure. With the release of the Savitz results, attention shifted sharply to magnetic fields, and worldwide interest in potential health effects from EMF exposure grew virtually overnight. Magnetic fields were now regarded by the public as a ubiquitous, unexplored exposure that could potentially contribute to a variety of health risks and, moreover, could affect children. Health effects of concern included not only cancers of different types but also endpoints such as pregnancy outcomes and neurodegenerative diseases (e.g., Alzheimer's disease) related to both residential and occupational settings.

EPRI responded quickly to this turn of events, convening an advisory committee of scientific experts, expanding its technical staff, and launching a new research program. The new research included epidemiologic studies investigating leukemia in children and leukemia and brain cancer in a large cohort of 140,000 workers from five participating U.S. utility companies; laboratory studies of leukemia and other cancers in a variety of rodent bioassay models; and large residential and occupational magnetic field exposure assessment and engineering studies. One notable residential research effort was the 1000-Home Study, which provided insights into the sources and levels of residential magnetic fields that remain valid today. Not surprisingly, the major sources of residential magnetic fields were found to be outdoor distribution lines and residential grounding systems. Transmission lines were also a dominant source, but the fraction of homes affected was very small.

EPRI also initiated a field management program and developed instrumentation and soft-



According to EPRI's 1000-Home Study, magnetic field strength in U.S. residences is distributed roughly according to a classic bell curve. About 5% of residences in the United States have an average magnetic field above 3 mG (green area).

ware for characterizing electric and magnetic field environments. The EMDEX meter and its derivatives are now the standards for measuring residential and occupational magnetic fields, and EMF and TLWorkstation software have provided EPRI members with valuable tools for estimating both electric and magnetic fields in residential and occupational settings. Indeed, EPRI's efforts in measurement instrumentation were largely responsible for critical advances in exposure assessment and epidemiology.

To help transfer EMF measurement technology to EPRI's members, the program conducted the EMDEX Occupational Study and the EMDEX Residential Study from the late 1980s to the early 1990s. The studies benefited from extensive industry participation, with 55 companies involved in the occupational study and 39 in the residential study. The research provided insights into exposure levels in the power company workplace relative to exposures outside the workplace, and the range of exposure levels to be expected across the general population. The occupational survey indicated that power company workplace exposures exceeded those normally associated with environments outside the workplace.

At the federal level, Congress enacted the EMF Research and Public Information Dissemination (EMF-RAPID) Program in 1992, when it became clear that questions about EMF had attained a high profile in the scientific and public mainstream nationwide. The EMF-RAPID Program (supported in part by contributions from EPRI members) had three basic components: "1) a research program focusing on health effects research, 2) information compilation and public outreach, and 3) a health assessment for evaluation of any potential hazards arising from exposure to ELF-EMF [extremely low frequency EMF, which includes power-frequency fields]." The National Institute of Environmental Health Sciences (NIEHS) was charged with overseeing the health research and conducting a thorough EMF risk evaluation.

The 1999 NIEHS final report to Congress concluded that "the strongest evidence for health effects comes from associations observed in human populations with two forms of cancer: childhood leukemia and chronic lymphocytic leukemia in occupationally exposed adults." This conclusion was qualified with the following statement: "The lack of connection between the human data and the experimental data (animal and mechanistic) severely complicates the interpretation of these results."

Two years after submission of the NIEHS report, a panel of experts at the International Agency for Research on Cancer (IARC), a branch of the World Health Organization (WHO) and the world's foremost agency concerned with cancer risk assessment, conducted an evaluation of the scientific literature on EMF and, specifically, its potential link to cancers of all types. The panel's deliberations were strongly influenced by two analyses of the EMF–childhood leukemia literature that were published in 2000, one by a group of scientists in the United States and the other by a group of European scientists. Both groups arrived at the same fundamental conclusion: that childhood leukemia incidence was associated with average residential magnetic fields above 3–4 mG (0.3–0.4 μT), with an approximate doubling of risk above this range of exposure levels. According to EPRI's 1000-Home Study, about 5% of residences in the United States have an average magnetic field above 3 mG, and less than 3% are above 4 mG. The magnetic field from a heavily loaded transmission line will fall off to less than 3 mG about 500 feet from the line, with correspondingly lower exposures for a lighter electrical load.

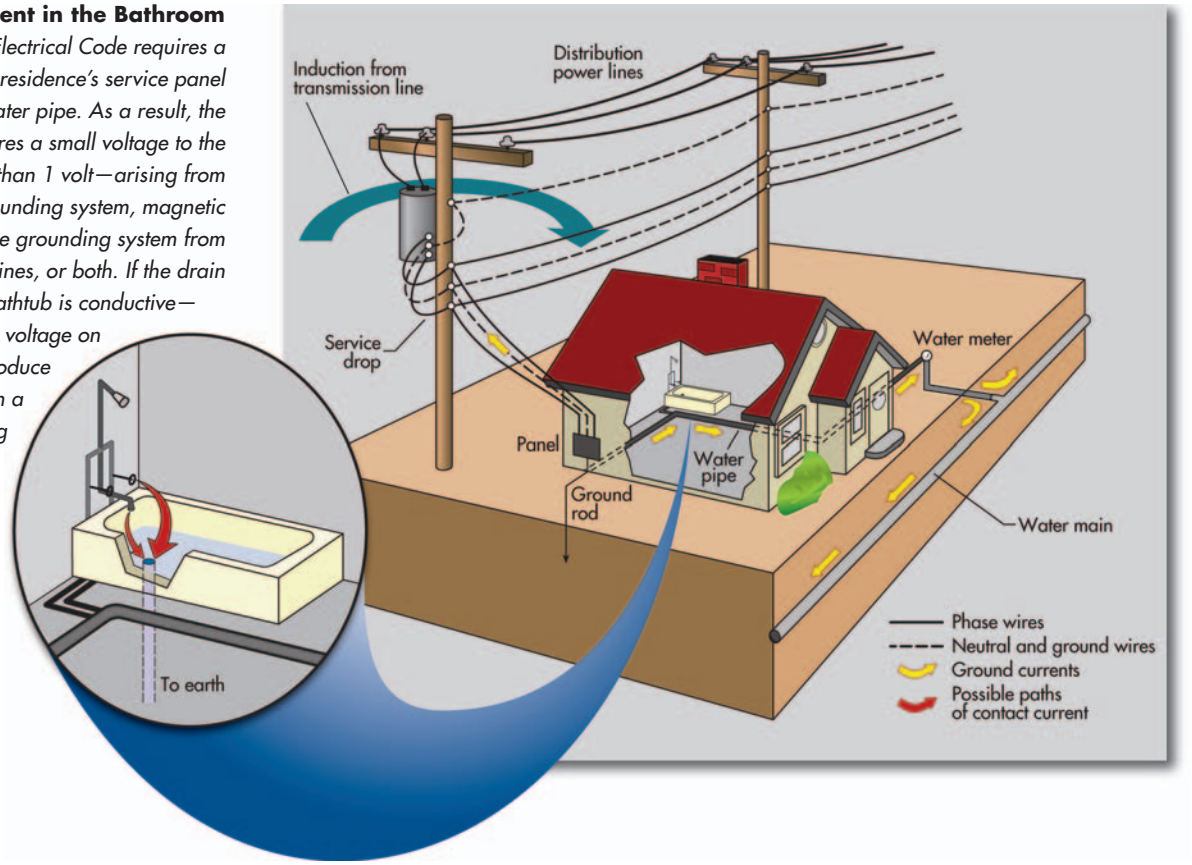
The IARC panel concluded that magnetic fields were a "possible" (IARC category 2B) human carcinogen, based on the "limited" evidence on childhood leukemia from epidemiologic studies and the lack of supporting evidence from cell and animal studies. The evidence concerning all other cancers was insufficient to form a basis for IARC's conclusion. To put this classification in perspective, coffee, pickled vegetables, chloroform, and welding fumes are among over 200 other exposures included in IARC's "possible" carcinogen category. IARC stated that the association between childhood leukemia and magnetic fields was not likely to be due to chance but conceded that epidemiologic artifacts could not be excluded. IARC also evaluated power-frequency electric fields, which by then were incorporated into several residential and occupational epidemiologic studies; electric fields were classified as a category 3 exposure (not classifiable as to carcinogenicity in humans), since the evidence was inadequate to assign even a "possibly hazardous" designation.

Other risk assessments have supported the IARC panel's conclusion. All the major assessments relied heavily on EPRI-sponsored research, and EPRI scientific staff were significantly involved in the panel deliberations held by both NIEHS and IARC. The presence of a credible industry-sponsored research program opened a seat at the table for EPRI. The next major development in EMF health assessment will be WHO's publication of its *EMF Environmental Health Criteria*, which will summarize and evaluate the relevant scientific literature and offer recommendations for further research. Scheduled for release in 2006, the report is likely to trigger a reassessment of research priorities, as well as further worldwide public interest in the EMF issue. Rob Kavet served as an observer to the final review of the report in October 2005, allowing EPRI to have a voice in the discussions and input to the final WHO report.

The credibility of EPRI's EMF health assessment work and the industry's commitment to research were highlighted in a September 2000 column in the *Wall Street Journal* by Marianne M. Jennings, a professor of legal and ethical studies. In contrasting other industries' approaches to well-publicized health and safety issues, she singled out the electric power industry's approach to EMF with praise, stating that "perhaps the best example of an industry willing to use the truth to set itself free was the electric utility sector. . . . EMF was managed with ethics and an attitude: If EMF is a problem, we manage it early and make it right. If it's a false alarm, we have the credibility and trust earned with voluntary action and disclosure at the moment of truth."

Contact Current in the Bathroom

The National Electrical Code requires a connection from a residence's service panel neutral to a nearby water pipe. As a result, the water pipe acquires a small voltage to the earth—usually less than 1 volt—arising from currents in the grounding system, magnetic field induction on the grounding system from nearby transmission lines, or both. If the drain in the residence's bathtub is conductive—made of metal—the voltage on the water pipe can produce a contact current when a person who is bathing touches the faucet or metal fixtures.



expected in the thinnest extremities, where the current densities must be the greatest —that is, in the lower arm and hand.

Evaluating Criteria for Plausibility

For contact current to be considered a viable candidate exposure that explained the epidemiology, investigators knew, three criteria would have to be satisfied prior to committing to further research: (1) a plausible dose to bone marrow, (2) a strong association of magnetic fields with the source of contact current, and (3) a child's frequent access to exposure. The failure to verify any one of the three would be a signal to stop this line of investigation.

Dose. If you discuss this issue with Kavet, he'll tell you that one of his heroes is a sixteenth-century scientist named Paracelsus, often referred to as the father of toxicology. Paracelsus put forward an idea that has become central to his field: Everything is poisonous in a high enough dose, and even strong poisons are harmless if the dose is low enough. In other words, "The dose makes the poison." Thus, to be a credible causal candidate, contact current would have to deliver a dose to tissue at levels that, according to biophysical principles, could plausibly elicit biological effects—a characteristic that residential magnetic fields did not provide.

Soon after the initial thoughts about contact current developed, the program teamed with Maria Stuchly and her research team at the University of Victoria to estimate the relationship of contact current exposure to electrical dose inside the body. Stuchly's research group already had extensive experience in using anatomically accurate computer models of the human body to estimate dose from exposure to EMF. The study, published in 2001, reported that small, imperceptible levels of contact current of the magnitude that could occur in the bathing scenario would produce doses in the arm's bone marrow that far exceeded (by factors of hundreds to thousands) the doses calculated from ambient magnetic fields; these were doses at levels that leaped over the hurdles that so challenged magnetic fields.

Association. Since the risk of childhood leukemia was observed to be greater in homes with fields above 3–4 mG, the higher values of voltage responsible for producing contact current—known as contact voltage—would necessarily need to coexist with these higher fields with a much greater probability than they would in homes with fields of lower values.

In 2001–2002, Kavet worked on the contact current idea with Enertech Consultants' Luciano Zaffanella, the architect of EPRI's well-known 1000-Home Study and the 1000-Person Study conducted for the U.S. Department of Energy as part of the federal RAPID program (see sidebar,

page 28). Zaffanella developed a protocol for characterizing the sources of contact current exposure in the home, as well as for taking routine measurements of the magnetic field, and applied them in a small pilot study for EPRI in Pittsfield, Massachusetts. The protocol focused largely on home appliances but also included measurements in the bathroom at all possible sites that people might touch on a routine basis. As it turned out, Zaffanella measured a significant voltage between the bath fixtures and the drain in the first two homes he visited.

Kavet and Zaffanella discussed the results the day the measurements were taken, becoming excited over the possibility that this voltage could be the missing link in the relationship between magnetic fields and childhood leukemia. The idea made immediate sense to the researchers: a bathing scenario meant that an immersed child's hand would be at least damp, if not saturated with water, which would reduce the skin's electrical resistance to an insignificant value. The small pilot study of 36 homes also reported data that suggested a positive association between the residential magnetic field and the voltage from the residential water line to earth, the source voltage for contact current exposure in the bath. This study's success triggered a larger effort in the Denver area, site of the two most important early EMF studies. In a measurement study that included visits to 191 residences, Kavet and colleagues reported a positive association between the residential magnetic field and both the voltage from the water line to earth and the voltage that a child would experience in the bathtub.

Though the measurement programs produced valuable data, they could not by themselves show how the infrastructural characteristics of communities would contribute to a set of empirical observations. Zaffanella and his associate Jeff Daigle, working closely with Kavet, produced the Contact Voltage Modeler (CVM), a program that makes it possible to specify a neighborhood's features—its geography, electrical distribution system, and water system—and then to identify the factors influencing residential magnetic fields, the voltage from residential water lines to earth, and the interrelationship of the two. The results supported the hypothesis that if a broad variety of neighborhoods in an extended geographic region (like those in epidemiologic studies) were simulated, a strong relationship between the magnetic fields and the water-line-to-earth voltages would be observed.

Frequent Access. In addition to the induction of genetic or chromosomal anomalies that initiate carcinogenesis, the pathway to malignancy in most cases involves other influences and exposures that, though not genotoxic themselves, nudge the already-affected cells toward a malignant state. The past 60 years of cancer research has shown that exposures subsequent to the initiation stage need to occur on a relatively frequent or repeated basis to have noticeable effects. Thus any exposure being considered as responsible for associations with magnetic fields would also have to occur reasonably often.

Anecdotally, many parents may recall that their young children, while bathing, indulged in exploratory play with the water fixtures or the water stream. Working with researchers at the University of California at Berkeley, EPRI supported a survey of parents using interview and diary techniques to assess the extent to which children from younger than one year to five years old engage in behavior that would produce exposure. The results indicated that roughly 80% of the children studied indeed displayed evidence of such behavior, and that beyond the age of one (when their arm's reach lengthened), this behavior increased.

The Testing Phase

With the criteria of dose, association, and frequent access satisfied, EPRI's research into the contact current hypothesis has accelerated from the plausibility phase to hypothesis testing by means of a multidisciplinary strategy. In 2003, the program joined forces with the School of Public Health at UC Berkeley, which since 1995, under the leadership of Patricia Buffler, has been conducting the Northern California Childhood Leukemia Study, the most intensive U.S. investigation yet of the environmental, genetic, and biochemical risk factors for childhood leukemia. The merger is a true bonanza for the EPRI program, not only allowing research into contact currents and magnetic fields but offering the program a significant opportunity to expand its research into control selection bias as well.

In 2006, following a competitive bidding process, EPRI began research at UC San Francisco with Scott Kogan to develop a genetically engineered mouse that will model the pathological events that lead to leukemia in children; ultimately this model will be put to the test with contact current exposures. Finally, the program is adapting the CVM to characterize exposure scenarios in countries where influential EMF studies have been reported, including both Sweden and the United Kingdom. The results of these efforts will emerge within the next five years and, when factored in with other research developments around the world, will determine future directions for the program.

A critical component of the EPRI program today, as for the past 18 years, is the advice and counsel of an independent advisory group of eminent scientists. The Scientific Advisory Committee meets on an annual basis to thoroughly review the program and offer recommendations. The committee remains informed of significant developments year-round and maintains an active relationship with the members of the program's Area Council. Working together with all of its advisors, EPRI's EMF health assessment program is committed to unraveling the critical uncertainties to ensure that electric and magnetic field environments are compatible with public health and safety.

Background information for this article was provided by Rob Kavet (rkavet@epri.com).