6. Cancer and Electromagnetic Fields: Epidemiological Studies

Cancer incidence in children and cancer as related to occupational ELF field exposure are the two areas that have received the most attention in the context of public health consequences of exposure to ELF fields. This concern with cancer arose as a result of an epidemiological study and has increased as several additional epidemiological studies have examined the association between ELF field exposure and cancer. The suggestion is not that 60 Hz fields initate cancer but rather that exposure to fields may serve to promote cancer once it is initiated by other causes (See endnote on promotion).

As biologic knowledge about an epidemiologic hypothesis is often missing or minimal, causal inference is hard to make. At the same time, public health problems or public perception of potential health problems may cause an action to be taken by decision-makers, despite imperfect knowledge about cause. Hill [Hill 65] developed a set of criteria by which to sort out causal from noncausal associations. These are :

1. Strength of association : that is, magnitude of the ratio of incidence rates in exposed populations to that in non-exposed, for example, the relationship between higher levels of smoking and lung cancer.
2. Consistency : Observation of same association in different populations under different criteria, for example, increased lung cancer incidence in smokers of all age groups, and races.
3. Specificity : single rather than multiple effects, as for example, when all the females exposed to DES prenatally exhibited the incidence of **a** particular type of cancer.
4. Temporality : Cause should precede effect in time.
5. Biologic gradient: That is, a dose-response relation or **a** definite mathematical relation between the amount of the exposure to an environmental agent and the incidence of the effect.
6. Biologic plausibility and coherence : A potential mechanism and an absence of conflict between the association and with what is known about the history and biology of the disease.
7. Experimental evidence : Particularly, animal data that points to the same association. This may not always hold . For example, some substances such as DES may not be carcinogenic in animals.
8. Analogy : If there is another agent that is analogous to the agent under consideration, and its biologic effect is well- (or better) known, we can look for analogous modes of action and effects.

In light of our discussion of “dose”, and nonlinear effects in Sections 3, criterion 5 above needs to be redefined and elaborated before it can be applied to ELF field exposure. Also, there is no analogous agent of the sort mentioned in criterion 8. Beyond this, we believe that the remaining criteria are directly applicable to epidemiological studies of ELF fields. At most, these considerations make the point that a further examination of the question through carefully designed, focused epidemiologic) studies are necessary in addition to laboratory experiments to understand the science before any firm conclusion can be drawn.

6.1. Childhood Cancer and ELF fields

Five completed epidemiological studies have addressed the question of association between exposure to ELF fields and cancer in children. These are all case-control studies. The Wertheimer and Leeper study [Wertheimer 79] in Denver first raised the question. The authors noted an association between childhood cancer and homes they classified as located near "high current configuration" distribution lines which were likely to produce stronger than average magnetic fields. The authors studied cases of children of age less than 19 years who died of cancer between 1950 and 1973, and who also had a Colorado birth certificate and resided in the area during most of their lives. The controls were children whose birth certificates placed "next" to the case children in the public birth files organized by birth month and county, except in the case when the "next" case was a sibling of a case child. 344 cases and 344 controls were examined.

After performing a series of measurements of magnetic fields to develop a simple classification scheme, the authors estimated the comparative magnitude of the magnetic field in the home by the surrogate measure of wiring configurations. Homes were classified as "HCC" and "LCC" (for high and low current configurations). A house was classified as "HCC" if one of the following conditions was satisfied : (1) it was close to a large gauge or several (6 or more) thin primary current-carrying wires from distribution transformers; (2) it was close to 3 or more thin primaries or high voltage (50kV to 230kV) lines, (3) it was less that 15 meters of wires coming directly from a transformer. A series of field measurements was performed to confirm these classifications.

The results showed that children exposed to a HCC configuration residential environment had a 1.6- to 2.2 -fold higher incidence of cancer than controls. Background incidence rate for childhood leukemia in children between the ages O to 14 years is about 10 in 100,000 per year [Greenberg 85]. If the children exposed to HCC configuration have a risk of 1.6 to 2.2 (or, about 2), relative to this background rate, this means that the risk of children exposed to HCC is double the base rate, or 20 in 100,000 per year. The study ruled out socioeconomic class, family pattern and traffic congestion near homes as possible confounders but did not deal with other possible factors that could cause confounding or bias. The results have been widely debated and criticized since their publication [Cole 87, Savitz 87b]. Among the limits of the study are : biases due to survival aspects introduced by studying only the cancer deaths rather than all cancers diagnosed; bias introduced by residential mobility; validity of the exposure measure; and, failure to account for other confounders.

Four studies have been done since the Wertheimer and Leeper study. Two of them found no association between leukemia and estimated exposure to magnetic fields. These two studies were conducted in Rhode Island [Fulton 80] and in Yorkshire, England [Myers 85]. The Rhode Island study included 119 childhood leukemia incidence cases and 240 controls, and was similar in design to the Wertheimer and Leeper study. The study in Yorkshire looked at all children diagnosed with cancer during 1970-79, a total of 376 cases and 591 controls. Residence classification was first made in terms of proximity to overhead power lines. Among those of the homes within I00m of the power lines, magnetic fields were estimated. There was no relationship observed between cancer incidence and either exposure metric.

Two other studies found positive results. The first of these was done in Sweden [Tomenius 86]. All 716 children diagnosed with cancer, and born and raised in Stockholm County during 1958-73 were included in the study. Tomenius found that there were more electrical constructions near dwellings of children who had cancer than of controls.. A single measurement of magnetic field near the front door was also taken for each house. There was no difference between the average value of magnetic fields at the doors of homes that were near electrical constructions or 200-kV lines and those that were not. However, magnetic fields at the door of homes within 150 m of 200 kV lines were higher than at the houses that did not have such lines close by. It was found that homes of cancer cases were twice as likely to have a front-door measurement of 3 mG or above than those of controls. The strongest odds ratio of 3.7 was noted for nervous system tumors.

The latest and by far, the most thorough and complete study is that by Savitz et al. [Savitz 87a, Savitz 88]. The study was designed to be similar to that of Wertheimer and Leeper, but with particular attention paid to several factors that were weaknesses in the former study. These were: a complete set of incident cases because of the use of the registry; use of a general population control group; expanded and detailed exposure measurement; and, measurement of possible confounding factors.

The Savitz study involved children from the Denver Standard Metropolitan Statistical Area of age 15 or less diagnosed as having cancer during the period 1976 to 1983, a period distinct from that of the Wertheimer and Leeper Study, which covered 1950 to 1973. Both wire coding and actual measurement of fields in the house were used to characterize the residential field environment. Detailed questionnaires elicited information about socioeconomic and other possible confounding factors such as smoking. An analysis of the total childhood cancers occurring in the Denver area children was also done and showed that Denver area children show the same overall risk **as** those in the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program.

Electric and magnetic fields data at three different times in a child’s chronology were selected for measurements and exposure assessments: the fields in the residence of birth to reflect early-life exposure; those at two years before the diagnosis to examine an effect of the field in promoting cancer; and, those at diagnosis. For each of these three times four types of field measurements or estimates were made : (1) magnetic field in the house when electric power consumption was low, (2) magnetic field in the house when electric power consumption **was** high, (3) electric field in the house when electric power consumption **was** high, and (4) the distribution system wire code classification using the system developed by Wertheimer and Leeper. An array of field measurements - fields in different rooms, variation over the day, etc. - **was** done. In fact, this part of the Denver study, conducted by Barnes and Wachtel [Barnes 87] has become a prime source in understanding fields in the home (see Section 2.2). For each power range, measured levels of magnetic fields were classified into four ranges : less than 0.65 mG, 0.66 to 0.99 mG, 1.00 to 2.49 mG and 2.50+ mG. Wire coding was used as a proxy for the long-term magnetic field level after it was calibrated using measurements.

The study also assessed other measures of potential field exposures such as electric heat and hot water use, use of water beds, heating pads and electric blankets by the children and by mothers during pregnancy and the total number of electrical appliances in the house. The results showed that the highest field (2.5+ mG) group in each power category showed a increased risk of about 20 to 60% above the controls for all cancers. The values for risk correlated with fields at two years before exposure and at time of diagnosis were similar. The odds ratio in this study **was** computed by taking the ratio of cancer incidence in each field group to the lowest (< 0.65 mG) group. The Odds Ratio (OR) for a group is a measure of how much more likely a child in that exposure group is to have cancer compared to a child in the lowest exposure group. The general results are summarized below:

Table 6-1.—Methodology and Results of Epidemiologic Studies of Childhood Cancer and Electromagnetic Field Exposure (Savitz 87a)

	Wertheimer & Leeper (1979)	Fulton et al. (1980)	Myers et al. (1985)	Tomenius (1986)
Geographic source	Colorado	Rhode Island	Yorkshire (England) Health District	Stockholm County
Case group:				
Time period	Deceased 1950-73	Onset 1964-78	Diagnosed 1970-79	Registered 1958-73
Diseases	All cancers	Leukemias	All cancers	All tumors
Age range	O to 18	0 to 20	0 to 14	0 to 18
Size	344 (491 dwellings)	119 (200 dwellings)	376	716 (1,172 dwellings)
Other criteria	Colorado birth certificates; resided in Denver area, 1946-73	Identified at Rhode Island Hospital: Residences up to 8 years before diagnosis	—	Born & diagnosed in Stockholm County
Control group:				
Source	Birth certificates	Birth certificates	Birth certificates	Birth certificates
Matching	Year of birth; some by county	Year of birth	Time of birth, near case's birth address	Age, sex, church district
Size	344 (472 dwellings)	240 (240 dwellings)	501	716 (1,015 dwellings)
Other criteria	Subsets formed based on residence information	Only birth addresses considered	Only birth addresses considered	Birth & "diagnosis" address in Stockholm
Exposure:				
Definition	Wiring configurations (wire type, gauge, number, proximity to home)	Estimated exposure from Colorado measurements, divided into quartiles	Calculated magnetic fields from overhead lines	Electrical constructions within 150m including 200-kV lines; 50-Hz magnetic fields near door
Range	Up to 35mG	N.A.	0.002 to 16.8mG	0.004 to 19mG
Potential confounders	Age of onset; sex; urban-suburban residence; socioeconomic class; maternal age; birth order; traffic density	Year of birth; father's socioeconomic level; age of onset	Age	Age, sex, church district
Results	Positive association between high-current configurations and cancer; dose-response gradient; consistent across cancers	No association observed between imputed exposure & leukemia	No consistent tendency for higher exposures among cases	More electrical constructions within 150m of case homes; more case homes >3mG

1. A **30%** increase in risk (Odds ratio= 1.31) for all cancers was observed at fields in the category 2.50mG + but none was observed in the two field ranges below (0.66 to 0.99mG and 1.00 to 2.49mG). The odds ratio did not systematically increase or decrease with the field magnitudes. That is, the higher the field ranges did not always give a higher cancer risk,

2. Cancer subgroups were analyzed under the categories, leukemia, lymphoma, brain tumors, soft tumors and "other cancers'*. All the categories except leukemia showed odds ratios 1.3 to 1.6 at high (2.5 mG+) field exposures only, Leukemia showed an odds ratio of 2.11 for the highest field class and 1.23 for the next one below.

3. The risk of cancer was not associated with measured magnetic field values at residence of birth.

4. For the one category (high-power) of electric field ranges analyzed, no association of the electric field categories with the odds ratio for cancers was found. That is, higher electric fields did not show higher risk of cancer.

5. Comparing odds ratio HCC/LCC of wiring configurations, odds ratios between 1.5 and 2.1 was found for all cancers with the highest 2.10 occurring for leukemia.

6. The results on the relationship of childhood cancer to use of appliances, electric blanket and waterbed, and electric heat are mixed but suggestive of a few trends. It must be remembered that the number of cases in the sample is small :

   a. Electric heat in residence and electric hot water:
   Lymphoma and cancers other than leukemia, brain, and soft tissue had odds ratio above 3.5, associated with electric heat in residences at birth, 2 years before diagnosis and at diagnosis. Leukemia showed elevated odds ratio for electric heat in residences two years before diagnosis, but not for electric heat for residences at birth and at diagnosis. Electric hot water in the residence showed no association with any of the cancers.

   b. Electric blanket, heated waterbeds, heating pad and total number of electrical appliances used by mother during pregnancy:
   Although electric blanket and water beds are known sources of high fields for in utero exposure, Savitz found no indication of increased cancer risk associated with such exposure. Heating pad use was associated with brain and soft tissue tumor cases. High appliance use was associated with soft tissue tumors, this relationship showing a monotonic increase in number of cases with increased appliance use from an odds ratio of 1.72 for 3-4 appliance use to 3.98 for 7 or more appliances compared to low (O-2) appliance use.

   c. Childhood appliance exposure:
   Electric blanket and isolette exposures were associated with increased risk of all cancers especially of the brain and soft tissue for isolette exposure.

Cole (1987) points out that the hypothesis of ELF magnetic fields **as** promoters or as growth enhancers would lead one to expect the average age of the highly exposed children in the childhood cancer studies would be lower than that for the control group. This, however, does not seem to be the case. Wertheimer has, however, argued that this lack of early appearance of cancer may be an artifact arising from the fact that if the promotion is pre- or perinatal, the fetal survival rate might have been affected and one might be seeing only a fraction of the affected children surviving to manifest the clinical cancer stage.

6.2. Residential Exposure and Adult Cancer

Three studies have examined the association between adult cancer and exposure to ELF fields from non-occupational sources, two in the U.S. examining residential exposures and one in England examining the proximity of residences to electrical transmission facilities.

Wertheimer and Leeper were also the first to report an association between adult cancers and residential wiring configurations in 1982 [Wertheimer 82]. They used a methodology parallel to the childhood cancer study described above. Four categories of wiring configurations were used to characterize residences in which the subject had lived for periods from three to ten years prior to the diagnosis of cancer. The authors reported an association between cancers of the nervous system, uterus and breast with a systematically increasing risk for higher current configurations. The strongest association was found for those subjects who had been in the coded residence for three to six years right before diagnosis and no association was found when the subjects had left the residence three years or more prior to it. Leukemia was not considered. The study also did not look for confounding factors and exposure determination was not done blind. When a study is not done blind, a bias on the authors' part to find an association might lead to a false positive result. Cole [Cole 87] notes that there is a "remarkable consistency" about the demonstrated relationship in the study. He remarks such a consistency is atypical of epidemiological studies even when a causal relationship actually exists, because of the large uncertainties that accompanies the data.

Stevens and coworkers [Stevens 87] at Battelle Pacific Northwest National Laboratories carried out a case-control study under the New York State Power Lines Project. Acute nonlymphocytic leukemia (ANLL) incidence was chosen as the effect to study because several of the occupational studies had indicated an association of ANLL incidence with occupations involving ELF field exposures. Wiring configurations and residential field measurements over 24 hour periods were used to characterize residential exposures. The cases of ANLL used were those registered at the Cancer Surveillance System at the Fred Hutchinson Cancer Research Center in Seattle, Washington. Cases of ANLL occurring in three counties in persons between 20 and 79 years of age and diagnosed in the period 1981 to 1984 were used, compared with controls generated by random-digit dialing. The study found no association between ANLL incidence and residential fields.

McDowall [McDowall 83] identified a cohort of people living in the vicinity of transmission lines and power substations in East Anglia in England and did a followup mortality study from 1971 to December 1983. He found no increased leukemia mortality incidence for this population compared to national or regional mortality rates.

These three studies were varied in concept and have several problems, such as confounding variables and uncertainties in the amount of field exposure, and do not provide enough evidence to judge the possibility of an association between residential field exposure and adult cancer.

6.3. Occupational Exposure and Cancer

We now discuss the studies of occupational exposure to ELF fields and the association with cancer in three categories, those examining associations with Leukemia, with brain cancer and with all cancers. Savitz and Cane [Savitz 87b] have reviewed the leukemia studies.

About twenty studies have looked for an association between cancer, particularly leukemia and brain cancer and occupational exposure to ELF fields. Studies have been done using electrical worker populations or ham radio operators in the U. S., England, Sweden and New Zealand. All except 5 Swedish studies have been proportionate mortality or morbidity studies or case-control studies. The five Swedish studies are retrospective follow-up studies which tend to be more reliable than proportionate mortality studies. The results of all studies taken together indicate **a** small positive association or no association.

6.3.1. Leukemia

Four occupational studies of U.S. male populations looked at leukemia deaths of "electrical" occupations as the end-point and calculated proportional mortality ratios [Milham 82, Wright 82, Cane 83, Milham 85]. Additionally, two U.S. studies of causes of cancer deaths [Peterson 80, Dubrow 80] yielding data for the association between leukemia and occupational ELF exposure have been examined by Savitz and Cane in their review article. Two studies from England and one from New Zealand have examined leukemia incidence in electrical workers. Leukemia was also examined in three retrospective follow-up occupational exposure studies done in Sweden [Olin 85, Barregard 85, Tornqvist 86]. Some of these studies also sorted out the incidence of or death rates from acute leukemias. Table 3 from the paper by Savitz and Cane [Savitz 87b] presents the results of their calculations combining data from eleven of the studies to obtain relative risk (RR) associated with specific electrical occupations, and the relevant confidence levels.

In Table **6-2, the highest** RR's -- for electrical equipment assemblers and aluminum workers have large uncertainties associated with them. The third group -- telegraph, radio and radar operators -- for whom the largest data set was available, show a consistently increased risk (RR = 1.8). The other sets showing RR's above 1.5 consisted of relatively small numbers of cases. There is a relative enhancement for acute leukemia in the top four groups.

Cole's review of epidemiologic studies include two additional case-control studies of the association between occupational ELF field exposure and leukemia [Cole 87]. One of these is **a** study of Swedish acute myelogenous leukemia cases among electrical occupations [Stern 86] which found a RR of 3.8. The second is an analysis of nuclear shipyard workers data, looking for association between leukemia cases and electrical jobs which found a RR of 2.3 for myeloid leukemia and 6 for lymphatic leukemia.

Based on the set of studies discussed above, it is fair to say that there is an indication that occupational exposure in "electrical occupations" is associated with enhanced leukemia risk. Remember that "associated" means "occurs together with"; it does not imply a causative link. The job classifications do not clearly indicate the actual occupational exposure to fields. No confounding variables and household and other exposures have been taken into consideration in these studies. Savitz's table above also involves combining data from U.S. and non-U.S. populations which might add to the spectrum of confounding, although the effect of such addition would be to decrease rather than increase the risk numbers if there were no real association at all.

Collectively the studies do not provide good evidence that **ELF field exposure increases the risk of** leukemia. At the same time the evidence precludes categorical statements that no such risk exists.

Table 6-2: Comparison of Occupational Studies of ELF exposure and leukemia [Savkz 87b].

Total Leukemias, Acute Leukemias, and Acute Myelogenous Leukemias in Electrical Occupations*

	Total leukemias		Acute leukemias		Acute myelogenous leukemias	
Occupations	RR	95% CL	RR	95% CL	RR	95% CL
Electrical equipment assemblers	2.4	(1.0 4.8)				
Aluminum workers.	1.9	(1.2 2.9)	2:6	(1.3 4.6)	❑	
Telegraph, radio, and radar operators .	1.8	(1.4 2.6)	2.1	(1.3 3.3)	2.6	(1.4 4.4)
Streetcar, subway, and elevated railway motormen	1.7	(0.7 3.3)	<1	expected	—	
Power station operators	1.6	(0.8 3.0)	2.2	(0.6 5.7)	<1	expected
Electronic technicians	1.3	(0.9 1.8)	1.8	(1.0 3.0)	1.9	(0.8 3.8)
Power and telephone linemen	1.3	(1.0 1.6)	1.7	(1.1 2.5)	2.5	(1.1 4.9)
Electrical and electronic engineers . . .	1.2	(1.0 1.5)	1.8	(1.2 2.3)	1.9	(1.3 2.7)
Electricians	1.1	(0.9 1.2)	1.1	(0.9 1.4)	1.0	(0.7 1.5)
Motion picture projectionists	1.1	(0.5 2.2)	1.2	(0.1 4.5)	<1	expected
Telephone repairers and installers	0.9	(0.6 1.3)	1.1	(0.6 1.8)	1.0	(0.4 1.8)
Welders and frame cutters	0.9	(0.7 1.2)	1.0	(0.7 1.5)	1.7	(0.5 4.5)
Total	1.2	(1.1 1.3)	1.4	(1.2 1.6)	1.5	(1.2 1.8)

● Abbreviations used are: RR, reliative risk; CL, confidence limits.

6.3.2. Brain and Central Nervous System (CNS) Tumors

The association between brain and CNS tumors and ELF field exposure related to occupation has been examined in about 10 studies, some of which are general cancer studies referred to in the above section on leukemia [Milham 85, Peterson 80, Olin 85]. Other studies looked specifically at brain and CNS tumor mortality risk in men with electrical jobs [Lin 85, Thomas 87] or at the association between cancer and electrical jobs or all jobs and sorted out the types of cancers [McLaughlin 87, Preston 82, Thomas 87, Vagero 83, Vagero 85].

Brain cancer is rare (1% of all cancer incidence, implying a risk of 5 in 100,000) in adults, peaking at about 60 years of age with a histology different from that seen in children in whom brain cancer is the second high-risk cancer (20°/0 of the cancer occurring in the age group O-8 years) peaking at about 5 years [Gold 79, Russell 71]. The small numbers of occurrence of brain cancers in adults poses a data problem in establishing causal association. The brain is also a favored site for metastasis[16] and hence

[16]Metastasis refers to secondary growth of cancer that spreads from a primary site.

cases counted as primary brain cancer may actually be secondaries spreading from a different organ in which the cancer was actually initiated.

Separate studies by Lin and Milham in 1985 were the first to suggest an association between brain/CNS tumors and occupational exposure to ELF fields [Lin 85, Milham 85]. Lin's case-control study is exceptional in the set of all occupational studies because he sought to correlate the brain tumor risk (RR) derived from death certificate data with the likelihood of exposure on the job. Based on occupational data from Maryland for 1974 to 1984, Lin obtained a relative risk of 2.2 for jobs with "definite" exposure 2.0 for those with "probable" exposure, 1.4 for "possible" exposure, and 1.0 for "no" exposure compared to age matched deed controls. His results indicate statistical significance, consistency, and an association between higher doses and higher risk of brain tumor.

Thomas and colleagues at the National Cancer Institute used death certificate data from northern New Jersey, Philadelphia and southern Louisiana to do a case-control study of the association between brain tumor mortality risk and electrical jobs, and found that data when all electrical jobs were combined showed an excess risk for astrocytic tumors (RR = 3.9). But his group included engineers, teachers, technicians, repairers and assemblers. When the data for electric manufacture and repair workers were separated, this high risk remained (RR = 4.9; 95% CI = 1.9, 13.2) and increased tenfold among those employed for 20 or more years. Data for electrical tradesman (electrician; power and telephone lineman) showed no statistically significant increased risk. The authors conclude that although ELF field exposure cannot be definitely or uniquely identified **as** an causative agent, some aspect of the manufacturing and repair jobs mentioned above does place the workers at increased risk of brain tumors.

All the studies of Swedish workers [Vagero 83, Vagero 85, Olin 85, Barregard 85, McLaughlin 87] saw no excess risk for CNS or brain cancer in electrical occupations.

Lin has also completed a study of employees of the electric power industry in Taiwan by an examination of the death certificates between 1971 and 1985. He observed an elevation of liver and brain tumors and leukemia with odds ratios in the range 1.3 to 2 [Lin 87].

Estimation of exposure is the main problem with these studies which use data based on occupational classification. The data are classified by job titles or general occupational codes. These "electrical occupations" in some cases include electrical and telecommunication engineers who are no more exposed to ELF fields than the average individual. Even electricians often work with circuits turned off so that their exposure may not be significantly different than that of others. In addition, these jobs often involve exposures to other environmental agents such as chemicals, and this can confounds the findings.

6.4. General Conclusions on the status of understanding of the ELF fields-cancer association

The question of association between cancer and ELF electromagnetic fields first arose because of the work on childhood cancer in Denver. Studies since then have yielded mixed results. The most thorough epidemiological study by Savitz and the cellular level studies described in Section 3 provide some evidence to support the possibility that ELF field exposure can act as a cancer promoter. Overall the evidence now available is too weak to allow firm conclusions either way, Because epidemiological studies involve human populations, they do not have the problems associated with extrapolating from cell to whole animal or from animal to human. On the other hand, the epidemiological studies which have been completed todate are all retrospective and so may involve confounding effects and bias arising from such lack of control. Prospective epidemiological studies which can be expected in the future, will have fewer such difficulties, but even in this case, because the subjects are people with several other activities to pursue, problems of control will remain. No single epidemiological study can demonstrate causation. But a series of carefully designed studies which all indicate a positive association can provide persuasive evidence for causation especially if there are also supportive cellular and animal data. If 60 Hz fields do pose cancer risks, it will be some time before this stage of understanding is reached. A number of improved epidemiological studies will be needed and more importantly, a series of animal cancer promotion studies will be needed. Largely because of limited research budgets, no animal promotion studies have yet been completed.