Historical evidence that residential electrification caused the emergence of the childhood leukemia peak.

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#### SUMMARY

A peak in childhood leukemia, ages two through four, emerged de novo in the 1920s in the United Kingdom and slightly later in the United States (US). Electrification in US farm and rural areas lagged behind urban areas until 1956. In recent years, childhood leukemia has been associated with residential electromagnetic fields. During 1928–1932, in states with above 75% of residences served by electricity, leukemia mortality increased with age for single years 0–4, while states with electrification levels below 75% showed a decreasing trend with age (p=0.009). During 1949–1951, all states showed a peak in leukemia mortality at ages 2–4. At ages 0–1, leukemia mortality was not related to electrification levels. At ages 2–4, there was a 24% (95% confidence interval (CI), 8%–41%) increase in leukemia mortality for a 10% increase in percent of homes served by electricity. The childhood leukemia peak of common acute lymphoblastic leukemia may be attributable to electrification.

### BACKGROUND

In 1961, Court Brown and Doll [1] suggested that, "...a new leukemogenic agent ...", had been introduced first into Britain in about 1920, and later into the United States and other countries. This was based on the remarkable observation that a new peak in childhood leukemia mortality between ages two and four had emerged in Britain in the 1920s and that in the fifty years starting in 1911, leukemia mortality had increased an average of 4.5 percent per year at ages under 10. They noted that the childhood peak was not present in mortality data for US blacks or in Japanese children. In the US, a leukemia mortality peak between ages two and four was first demonstrated in hospital data by Cooke in 1942 [2], but years of death of the cases were not specified. In a 1958 review of US leukemia mortality, Gilliam and Walter [3]. demonstrated a childhood peak for white boys dying in 1929–1931, and for white girls dying in 1939–1941. They did no analysis for intracensal years, 1932–1938. No such peak was evident for black children. For the years 1921–1955, they also showed a dramatic increase in the age-adjusted leukemia mortality rate for all ages in both whites and non-whites and in both sexes. For the entire US population, leukemia increased by 64 percent between 1930 and 1940, and by 43 percent between 1940 and 1950. Fraumeni and Miller [4] demonstrated that the childhood peak, missing in US blacks and in the Japanese in earlier years had emerged in both groups after 1960. They also demonstrated that after 1955, leukemia rates in the US and in England and Wales have tended to level off. Burnett, in 1958 [5] commented that whatever was causing these changes in leukemia mortality represented, "...some widespread change, not something peculiar to one country." In the last two decades, with the development of population-based tumor registries, it has been shown that there are ten-fold differences in the incidence of childhood leukemia around the world from a low of 0.4 per 100,000 in black African children to a high of about 4.5 per 100,000 in Hispanic children in Costa

Rica [6]. A number of authors have decided that the time trends and racial and ethnic differences indicate that common acute lymphoblastic leukemia (cALL) is somehow linked to an improving standard of living [7], increased socioeconomic status [8], increased industrialization, and urbanization of the population [9]. Greaves and Alexander [10, 11] discuss the evidence for in utero initiation of childhood leukemia and point out that cALL which arises from B cell precursors, makes up 75 percent of all childhood acute lymphoblastic leukemia and 60 percent of all childhood leukemia, and is solely responsible for the peak in childhood leukemia between ages two and five.

A number of theories explaining the etiology of acute lymphoblastic leukemia have arisen as the result of recent studies in Great Britain. Alexander [12], suggests a viral etiology, Kinlen [13], favors population mixing and an unusual exposure to a common infection, and Greaves and Alexander [11] favor immunologic isolation in infancy followed by a rare response to a common infection. Small area analysis supports the association between higher socioeconomic status of areas and the incidence of childhood leukemia. Rodrigues et al [14] and Greaves and Alexander [11] note that the area results are stronger than individually based results, suggesting that "....community characteristics are themselves of etiological importance."

Since 1979 there has been accumulating epidemiologic evidence that leukemia and certain other cancers are somehow linked with exposure to electromagnetic fields (EMFs). Wertheimer and Leeper [15] reported that Denver area children who had died of childhood cancers had visible electric wiring at their houses which differed from that at non-cancer comparison houses. The difference suggested that the cancer houses were served with higher electric currents, and therefore had higher residential magnetic fields. In 1982, one of the authors (SM) showed that occupations with an intuitive exposure to EMFs had increased mortality due to leukemia [16]. Since the early 1980s about 100 occupational and 40 residential epidemiologic studies of the EMF-cancer association have been published [17]. Interestingly, of the approximately 500 separate risk ratios published in these studies, six are elevated for every one that is reduced. A recent meta-analysis of 16 childhood leukemia studies [18] concludes that, "...the data provide relatively strong and consistent support for a somewhat weak elevated risk of leukemia for children living in proximity to power lines." A working group of the National Institute of Environmental Health Sciences recently decided that EMFs are probable carcinogens, and that the leukemia-EMF link demonstrated a "fairly consistent pattern" in epidemiologic studies of both children and electrical workers [17]. If some facet of EMF exposure is indeed carcinogenic, a simultaneous examination of the history of electrification and leukemia in the US should be revealing. Childhood leukemia with death under age 5 years was chosen as the cancer to study, because until about 1960, it was uniformly fatal, and was well reported on death records. Also, the descriptive epidemiology of childhood leukemia strongly suggests an environmental etiology [19]. We decided to concentrate on the early years of electrification in the US, since, in the developed world, electrical exposures are now so widespread that it is nearly impossible to find unexposed comparison groups.

In the US, in 1920, about half of urban and rural non-farm homes had electric service as compared to 1.6 percent of farm homes [20]. By 1940, 90 percent of non-farm residences had electric service compared to 35 percent of farm homes. It took until 1956 for farm homes to have the same percentage of electric service (98 percent) as non-farm homes. The great distances and expense delayed rural electrification in the US until the Rural Electrification Act was passed in 1935. The delay of a generation in the electrification of farm homes in the US created an opportunity to examine the epidemiology of leukemia in this time period in relationship to electrification. Interestingly, as late as 1955, only 20 percent of generated electricity was used in residences [20].

#### MATERIALS AND METHODS

Mortality records of the US, 1920–1960 [21] and US census bureau data (US Census of population, 1930, 1940, 1950) for populations and electrification [20] were examined, abstracted and keyed. Childhood leukemia deaths by year, state, race and age (single years of age through age four) and state population data were entered into a personal computer. National data was available for all years, but state data by single years of age was only available for years around the 1930 and 1950 censuses. Additional US Bureau of the Census population data was downloaded from the Internet [22]. Poisson regression was used to study the relationship between electrification and leukemia mortality. S-Plus [23] was used for analysis.

For 1940 and 1950, the percentage of homes by state with electricity is available for three classes of homes: urban, rural non-farm and farm. For 1930, only the number and percentage of farm homes by state with electric service is available. The 1930 urban and rural non-farm electrification levels were estimated by applying the 1940 electrification data to the 1930 population data. On the national level, there was little change between 1930 and 1940 in the percent of urban and rural non-farm homes with electric service [20]. These estimates are certainly higher that the true 1930 data, since electrification rates were higher in 1940 than 1930.

Childhood leukemia rates by single years of age through age four were calculated for each state 1928–1932 and 1949–1951 by using the annual death counts and the census population data for 1930 and 1950. Some states entered the death registration system during 1928–1932. For these states, the leukemia death rate was calculated using the years for which information was available. Data was missing for the following states in the years noted: Nevada, 1928; New Mexico,1928; South Dakota,1928–1929; Texas,1928–1932; and Alaska , all years. Hawaii entered the death registration system in 1929, but no state data was available for Hawaii.

White infant mortality rates by state for 1950 were compared to childhood leukemia mortality rates ages two through four, and to percent of residences served by electricity by state.

# <u>RESULTS</u>

The results are based on 1,333 leukemia deaths in children under the age of five in 1928–1932, and 2,640 such deaths in 1949–1951.

Figure 1 shows the development of the childhood leukemia peak for white children in the US in the period 1920–1960. No such peak is seen for black children in the same time period. During 1928–1932, states with a higher percentage of homes served by electricity had higher childhood leukemia mortality (see Figure 2).

For 1928–1932 the authors fit a model using state mortality data in five age categories (single years of age through age four) and state electrification data as percent of homes served. In this model electrification significantly modified the relationship between age and leukemia mortality (p = 0.009). Figure 3 shows the trend in leukemia mortality rates across age up through age four for five categories of electrification. In states with electrification levels of 75 percent or more, leukemia mortality increased with age while states with electrification levels below 75 percent showed a decreasing trend with age.

In the final model for 1949–1951 data, age was entered as a categorical factor with two levels, age less than two, and ages two through four, and electrification was entered as a linear factor. During 1949–1951, all states showed a peak in mortality at ages two through four (see Figure 4). The peak was highest in states with the highest levels of electrification. At age less than two, leukemia mortality was not related to electrification levels. At ages two through four, there was a 24 percent (95 percent confidence interval 8%–41%) increase in leukemia mortality for each 10 percent increase in percent of homes served by electricity. In 1950, in states with less than 95 percent of residences electrified, there was no relationship between white infant mortality rates and residential electrification, while these states clearly demonstrated the childhood leukemia peak association with residential electrification. Also, no association was seen between infant mortality rates by state and leukemia rates at ages two through four.

# DISCUSSION

The most remarkable feature of childhood leukemia has been the development of a childhood peak of incidence at ages two through four. This peak has been shown to be made up of the single leukemia subtype, common acute lymphoblastic leukemia. The results of our study suggest that the childhood leukemia peak was present in 1930 in the United States in states with more than 75 percent of residences served by electricity. By 1950, the peak was evident in all states, but was more pronounced in those states with a higher percentage of homes with electric service. In the non-peak ages less than two years in the years 1949–1951, childhood leukemia mortality rates were not related to electrification levels. Our results suggest the childhood leukemia peak occurred earlier in states with high levels of residential electrification.

World-wide, the emergence of this peak tracks electrification. Even today, places without electrification do not show this peak. Similarly, the association between social class, urbanization, modernization, and industrialization and leukemia incidence could all be explained by electrification. In an attempt to explain the shift from childhood lymphoma to leukemia which occurred in Gaza Strip Arabs in the 1970s, Ramot and McGrath noted dramatic increases in ".. available housing and owned appliances" and hypothesised that the environment "... is a major determinant...." of the childhood cancer patterns they observed. In the same time period Israeli Jewish children already showed the childhood leukemia pattern which Israeli Arab children were developing. Black Africans do not demonstrate the childhood leukemia peak, and in the early years of electrification, US blacks who were primarily rural without electric service, also did not show the peak. As electrification spread to rural areas, and blacks moved to urban (electrified) areas, blacks like whites demonstrated the peak.

The international pattern of childhood leukemia incidence reviewed by Linet and Devesa [19] also fits nicely with electrification. Costa Rica's high incidence is not surprising, since it has the health characteristics of developed countries and has a high level of electrification. The highest leukemia rates are seen in North America, Scandinavia, in New Zealand and Australian whites, and in Hong Kong. In small area studies in the UK, the fact that community characteristics outweigh individual characteristics in predicting leukemia risk, is consistent with an effect of electrification. The fact that the childhood leukemia peak was first seen in the UK, may be due to the fact that Britain and Europe electrified their farms much earlier than those in the US, and UK mortality registration was more complete at that time.

Power-frequency (50 and 60 Hz) alternating magnetic fields are the most likely active agents in the electrification effect. In the EMF literature, childhood leukemia incidence has been associated with historical calculated magnetic fields above one mG (milligauss) [24] and acute lymphoblastic leukemia incidence in children has been associated with measured magnetic fields above three mG [25]. Residential magnetic fields above one mG are uncommon today, and must have been rare in the early days of electrification. In the US in the period 1920–1940 electricity in homes was used primarily for lighting, with the radio and electric iron often being the only electrical appliances. With the great increase in appliance use after 1940, residential electric currents and magnetic fields must have increased. Residential power consumption rose by a factor of eight between 1940 and 1960 [20]. The delay in the appearance of the childhood leukemia peak until the 1930s may be due to the fact that residential magnetic fields were not high enough to induce leukemia until then. The rise in leukemia rates over time may reflect rising population exposure to alternating magnetic fields. Improved reporting of leukemia incidence and mortality could account for some of the time trend increase, but the emergence of the childhood peak would necessitate the unlikely scenario that leukemia at ages two through four was better diagnosed and ascertained than at other ages. Infant mortality rates by state, a surrogate for level of medical care and, therefore diagnosis and ascertainment of childhood leukemia, were not related to leukemia mortality in the peak years or to residential electrification. The fact that the childhood leukemia peak first appeared with electrification and is seen only in electrified areas suggests that a large percentage of childhood cALL is attributable to electrification. The leveling off of leukemia rates after 1950 may reflect the leveling off of residential magnetic field exposures. Modern home construction which uses non-metallic water and sewer pipes results in lower ground currents and residential magnetic fields. Similarly, the under-grounding of residential electric service results in lower residential magnetic fields.

It could be argued that some other new urban factor in the 1920s and 1930s caused the childhood leukemia peak to emerge when it did. However, this could not account for the fact that rural areas in the US developed the peak only after they received electric service while retaining their essentially rural nature. In the decade between 1930 and 1940 when the childhood leukemia peak first emerged, the urbanization of the US population increased less than one percent [20]. Kinlen hypothesized that population mixing caused by inward migration into a region and consequent unusual exposure to a common infectious agent could increase childhood leukemia incidence [13]. US Census data does not show larger population increases in regions with more electrification than in other regions

between 1920 and 1930 [20]. By 1950, the childhood peak was apparent in all states, including those where the population had decreased. Unfortunately, US states are too large to test the "new town" hypothesis.

In the US in the period 1920–1960, the great distances, sparse population in rural areas, and the great expense of electrification delayed the extension of the new world-wide technology of electric power into the population for a period of nearly 35 years. This resulted in two large populations, one exposed to and one not exposed to residential EMFs. Fortunately, both populations were covered by the same mortality registration system, and the large number and heterogeneity of the US states for which single year of age childhood leukemia mortality data was available allowed clear differences in childhood leukemia mortality to be seen.

Until poles and wires were first extended into our communities, humans had never been exposed to alternating power-frequency fields. Similarly, radio, television, radar, microwaves, cell phones, and the other indispensable devices of our modern world, all expose humans to EMFs which are completely new to human evolutionary experience. There is some evidence that other parts of the electromagnetic spectrum may be leukemogenic [26, 27]. Weak alternating magnetic fields have been shown to effect reaction time [28], slow the heart [29], and effect the electroencephalogram in humans [30]. Nocturnal secretion of the pineal hormone melatonin, a powerful anti-cancer agent, is suppressed by chronic exposure to alternating magnetic fields in electrical workers [31].

A criticism of the EMF/cancer epidemiologic studies is that calculated risks have usually been low (two or three times as high as expected). We believe that this is due to the fact that there are no truly unexposed comparison or control groups in developed (electrified) societies, and that EMF exposure assessment has been limited to the power-frequencies. The analyses of the twentieth century rise in residential electric consumption along with flat cancer and leukemia incidence in the US [32] and Canada [33] are often cited as evidence against any EMF -cancer association. Both analyses are seriously flawed, since they begin their cancer trend analyses in the 1970's, forty years after the childhood leukemia peak emerged.

We must ask why others who have studied the emergence of the childhood cALL peak did not arrive at the same conclusion. As early as 1960, Court Brown and Doll [1] recognized that a new leukemogen had been introduced into the UK and the US in the 1920s and 1930s, but did not make the connection to electrification. This is understandable in that none of the epidemiologic studies linking leukemia with EMFs had been done yet, and there was no evidence then that low energy power-frequency fields were either biologically active or carcinogenic. The urban-rural spread of leukemia in Europe happened over a much shorter time period than it did in the US, and in the US, where there was a long delay in rural electrification, the leukemia mortality data and US census data was missing or discontinuous for urban-rural status and for electrification. Before 1932, mortality data was available for only a fraction of the US population. There is no mention of urban-rural status in the otherwise detailed analysis done by Gilliam and Walter [3].

To follow up on our observations, childhood leukemia deaths before 1960 in the peak age years could be compared to childhood leukemia deaths at other ages to see whether they had in utero or early infancy exposure to an electrified residence. An area covered by a tumor registry which has a large number of electrified and non-electrified residences could examine cALL cases in the childhood peak in a similar design.

The authors conclude the childhood leukemia peak of common acute lymphoblastic leukemia (cALL) is attributable to residential electrification. Seventy-five percent of childhood acute lymphoblastic leukemia and 60 percent of all childhood leukemia may be preventable.

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Figure 1: Childhood leukemia mortality for US whites by single years of age 0–4, US, 1920, 1930, 1940, 1950, and 1960.



Figure 2: Childhood leukemia mortality rates in death registration states, all races, 1928–1932, by percent residential electrification and age at death. (States were grouped by quintile of percent of homes with electric service, and rates were computed for each quintile.)



Figure 3: Linear regression on childhood leukemia mortality rates in death registration states, all races, 1928–1932, by percent residential electrification and age at death. (States were grouped by quintile of percent of homes with electric service, and rates were computed for each quintile.)



Figure 4: Childhood leukemia mortality rates in all US states, all races, 1949–1951, by percent residential electrification and age at death. (States were grouped by quintile of percent of homes with electric service, and rates were computed for each quintile.)