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### **Exposure to Electrical Contact Currents and the Risk of Childhood Leukemia**

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#### **Abstract**

The objectives of this study were to examine the association between contact current exposure and the risk of childhood leukemia and to investigate the relationship between residential contact currents and magnetic fields. Indoor and outdoor contact voltage and magnetic-field measurements were collected for the diagnosis residence of 245 cases and 269 controls recruited in the Northern California Childhood Leukemia Study (2000–2007). Logistic regression techniques produced odds ratios (OR) adjusted for age, sex, Hispanic ethnicity, mother's race and household income. No statistically significant associations were seen between childhood leukemia and indoor contact voltage level [exposure  $\geq$ 90th percentile (10.5 mV): OR = 0.83, 95% confidence interval (CI): 0.45, 1.54], outdoor contact voltage level [exposure  $\geq$ 90th percentile (291.2 mV): OR = 0.89, 95% CI: 0.48, 1.63], or indoor magnetic-field levels  $(>0.20 \mu T$ : OR = 0.76, 95% CI: 0.30, 1.93). Contact voltage was weakly correlated with magnetic field; correlation coefficients were  $r = 0.10$  $(P = 0.02)$  for indoor contact voltage and  $r = 0.15$   $(P = 0.001)$  for outdoor contact voltage. In conclusion, in this California population, there was no evidence of an association between childhood leukemia and exposure to contact currents or magnetic fields and a weak correlation between measures of contact current and magnetic fields.

#### **INTRODUCTION**

Epidemiological research conducted over the past 30 years has indicated an apparent association between residential power-frequency (50–60 Hz) magnetic fields and childhood leukemia (1). In 2000, two pooled analyses (2, 3) reported statistically significant 1.7- to 2.0-fold increased risks of childhood leukemia in children exposed to residential magnetic fields over 0.3 or 0.4 μT compared to those exposed to magnetic fields under 0.1 μT. In 2002, based on the association with childhood leukemia, extremely low-frequency magnetic fields were classified as a possible human carcinogen (Group 2B) by the International Agency for Research on Cancer (4). Results from experimental studies, including rodent bioassays, do not support a link between magnetic fields and leukemogenesis (5, 6). Numerous explanations such as confounding, measurement error and selection bias have been explored, with no conclusive results (7–9).

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This study explores an alternate explanation; that is, exposure to contact current may act as a confounder in the reported associations between magnetic fields and childhood leukemia. To be a confounder in this relationship, contact currents would need to be associated with both magnetic fields and childhood leukemia. The aim of this research was to explore these relationships in an established California case-control study of childhood leukemia.

Contact currents occur when a person touches conductive surfaces at different potentials and completes a path through which electric current flows within the body. The voltage on a residential water line can produce contact currents in young children while they are bathing provided that they are in contact with a metallic fixture contiguous with conductive and grounded water pipes and that the drain is made of conductive material. In the only data set from a large-scale exposure assessment of residential contact voltage (10), about 4% of the residences had a contact voltage measurement of 100 mV or greater in the bathtub (data not shown). Assuming that a child's wet body resistance is 1,000 ohms (11), dosimetry modeling estimates that for an 18-kg child, the resulting current (100  $\mu$ A) would produce a 99th percentile electric field in the lower arm of 1.5 V/m (12).

Whether electric fields of this magnitude can influence lymphoproliferative dynamics and thus provide a possible impetus for leukemogenesis has not been tested. However, a likely site of interaction is the stromal matrix within the bone marrow, upon which reside the proliferating reservoir of immature lymphocytes that ultimately populate the mature immune system. The stromal cells, which are of the order of hundreds of micrometers long (13, 14), are responsible for orchestrating the maturation of the lymphocytic lineage through their ability to adhere lymphocytes to their surface while secreting mediators that regulate and coordinate lymphocytic development (15). One can estimate that a 1.5 V/m electric field in the marrow of a child's lower arm would transduce about 150 μV across at least a portion of the plasma membrane of a 200-μm-long cell. A transmembrane potential of this magnitude is associated with biological activity (16, 17). A lymphocytic stem cell roughly 6 to 8  $\mu$ m in diameter exposed to the same current would transduce a far smaller potential (approximately 7–10 μV) across its membrane.

By comparison, dose modeling predicts that the highest dose to the bone marrow of an 18 kg child from a 1-μT, 60-Hz magnetic field would induce no greater than 40  $\mu$ V/m in the bone marrow (18). An electric field of this size would result in about 4 nV across a 200-μm stromal cell's plasma membrane. The magnetic field's induced dose to marrow is thus orders of magnitude smaller than the dose from 100 mV contact voltage and is well below any stated threshold for biological activity. Therefore, based on prior evidence of a positive association of contact voltage with residential magnetic fields and on the fact that ambient levels of contact voltage can produce electric fields in children's bone marrow of a magnitude associated with biological activity, we investigated the hypotheses that exposure to contact currents may be associated with childhood leukemia or may confound the reported associations between magnetic fields and childhood leukemia.

#### **MATERIAL AND METHODS**

#### **NCCLS Study Participants**

Participants in the study of contact currents were a subset of cases and controls who participated in the NCCLS between March 2000 and June 2007. The NCCLS is a casecontrol study of genetic and environmental risk factors in the etiology of childhood leukemia that encompasses 35 counties in Northern and Central California. Incident leukemia cases were rapidly ascertained from nine major pediatric clinical centers usually within 72 h of diagnosis. Cases were eligible if they met the following criteria: (1) under 15 years of age at diagnosis; (2) a parent or guardian speaks English or Spanish; (3) residence in one of 35

California counties at the time of diagnosis; and (4) no previous history of malignancy. Approximately 77% of cases ascertained by NCCLS were eligible for the study, and about 86% of eligible cases consented to participate. The NCCLS case population consists of acute lymphoblastic leukemia (84%), acute myeloid leukemia (13%), and chronic myeloid and other leukemia diagnoses (3%). For each case, one or two controls were identified using California birth records, matched on date of birth, gender, Hispanic ethnicity (i.e., either parent is Hispanic), and mother's race (White, African American or other). Of the 2407 potential control subjects that we attempted to locate, 1263 (52%) were deemed eligible to participate in the study. Of those eligible, 1089 (86%) consented to participate. Overall this represents approximately 45% (1089/2407) of potential controls participating in the study.

#### **Contact Current Study Participants**

Study participants were cases and controls who previously participated in NCCLS home environmental sampling studies. Eligibility was restricted to subjects who resided in the same home since the diagnosis/reference date and were under age 8 years at diagnosis or reference date (the corresponding date for matched controls). Eligibility was limited to children under 8 because younger children tend to spend more time in the home and in the case of contact current measurements are more likely to take baths. To maximize the number of eligible children regarding the residential stability criteria, individual matching was not maintained. Age and residential stability criteria yielded 38.5% of the cases (257/667) and 35.6% of the controls (291/817), of whom 245 (95%) and 269 (92%) agreed to participate, respectively, in the household measurements. Written informed consent was obtained for each participating family, and study protocols were approved by the Institutional Review Board of the University of California, Berkeley and the Institutional Review Boards of all participating institutions.

#### **Exposure Assessment**

A pilot study was performed to assess the feasibility of characterizing the bathing behavior of young children. Forty volunteer families with children under 6 years of age completed a 10-day bathing diary. Results from the pilot study supported the critical assumption that children do have frequent contact with sources of electrical currents while bathing; physical contact in the bathtub (defined as touching the water spout and/or faucet) occurred while bathing 77% of the time for a child aged 1–6, with an average of one contact per bath. The feasibility of conducting residential contact voltage measurements (both point-in-time and long-term measurements) was demonstrated in prior studies (10, 19, 20).

Electrical contact current and magnetic-field measurements were conducted by engineering technicians from Enertech Consultants (Campbell, CA) over 4 years (2004–2007), during the late spring, summer and early fall (to maximize daylight hours for outside measurements). To control for seasonal variation in electricity use, 24-h outdoor temperature readings were obtained from the National Oceanic and Atmospheric Administration (NOAA) website. The outdoor temperature reading used in the analysis was the one closest to the time household measurements were made. Demographic data (gender, date of birth, date of diagnosis, race, household income and parental education) were available from the in-home parent interview.

**Contact current measurements—**Contact voltage between the faucet and drain in the bathtub most commonly used by the subject was measured using a voltmeter with a 1000 ohm resistor across the meter's leads to simulate human body resistance. Measurements were logged every 5 s for 30 min, and an average value was computed  $(V_{\text{bath}})$  and served as the primary exposure measure for assessing potential exposure to contact current. The secondary exposure measure for assessing potential exposure to contact current was the

voltage measured with a 1000-ohm resistor between the outside water service line and a metallic stake driven into the ground about 8 m away  $(V_{W-F})$ . Indoor contact voltage measurements were available for all but one residence, and outdoor contact voltage measurements were available for 476 (92.4%) residences.

**Indoor magnetic-field measurements—**Spot (or point-in-time) magnetic-field measurements were made at a convenient location 1 m from the floor and away from any electronic devices or electric appliances in the center of each room of the residence: kitchen, living room, dining room, family room, bathrooms and bedrooms. The room with the median magnetic field was selected for recording of power-frequency magnetic fields every 5 s for 30 min using the Emdex Lite. The average reading over the 30-min period ( $B_{avg}$ ) is the indoor magnetic-field measurement used in this study. Indoor magnetic-field measurements were available for all 514 residences.

#### **Statistical Methods**

Log values were used for correlation analyses and comparisons of means since the distributions of contact current and magnetic-field measurements were skewed to the right. Pearson correlation coefficients for continuous variables and Spearman rank coefficients for categorical variables were calculated among magnetic-field levels, indoor/outdoor contact voltage levels, and potential confounders such as income, race and residence type. Differences in mean values between cases and controls were assessed with two-sided *t* tests. Multivariable logistic regression analysis was used to examine the influence of contact voltage and magnetic fields on the risk of childhood leukemia, adjusting for age at diagnosis/reference date (continuous), gender, Hispanic ethnicity and mother's race as well as household income (ordinal), due to its association with both disease and exposure. Odds ratios and 95% confidence intervals were calculated using both continuous and categorical variables. Exposure categories were defined by the distribution of exposure in controls, using quartiles and a binary variable (above or below the 90th percentile). In addition, 0.2 μT and 0.3 μT were used as a threshold of exposure for  $B_{avg}$ , based on levels reported in the peer-reviewed literature (3, 21, 22).

Confounding was assessed for four groups of covariates: parental demographics (mother's and father's education), housing characteristics (residence and neighborhood type, year residence was built, urban/rural status and drain type), conditions at the time of the measurement (time of day, temperature, month and season), and time effects (time from diagnosis/reference date to measurement and duration of time in residence prior to diagnosis/reference date). Each covariate was added individually to the model and loglikelihood values were compared to identify potential confounders (*P* values less than 0.10 and a change in odds ratio of more than 10%). None of the potential confounders met these criteria and were not included in the final regression model.

#### **RESULTS**

Demographic characteristics of cases and controls (Table 1) indicate that cases were of lower socioeconomic status (SES) than controls as measured by annual household income  $(P = 0.01)$  and paternal education  $(P = 0.05)$  and were more likely to be of Hispanic origin  $(P = 0.07)$ . The mean time between diagnosis/reference date and measurement date was 23.7 months for cases and 32.1 months for controls ( $P < 0.01$ ; Table 2). Characteristics of the residential measurements indicated no statistically significant differences between cases and controls with respect to the year the house was built, urban/rural designation, time or season of measurement, temperature at measurement or residence type.

Differences in means assessed with *t* tests indicated no significant differences in the distribution of exposure variables for cases and controls; means of log-transformed values between cases and controls for B<sub>avg</sub> ( $P = 0.84$ ), V<sub>bath</sub> ( $P = 0.91$ ) and V<sub>W-E</sub> ( $P = 0.63$ ) are presented in Table 3. As shown in Table 4,  $V_{\text{bath}}$  appeared to be only weakly correlated with  $B_{\text{avg}}$  ( $r = 0.10$ ,  $P = 0.02$ ). A weak correlation was also observed between V<sub>W-E</sub> and B<sub>avg</sub> ( $r =$ 0.15,  $P = 0.001$ ), and the two contact voltage measurements were weakly correlated ( $r =$ 0.08,  $P = 0.09$ ). The year the house was built was correlated with B<sub>avg</sub> ( $r = 0.25$ ,  $P < 0.001$ ) and  $V_{\text{bath}}$  ( $r = 0.38$ ,  $P < 0.001$ ), with older houses having higher exposures.

Odds ratios comparing indoor contact voltage measurements  $(V_{\text{bath}})$  between cases and controls (Table 5) were close to 1.0 and were not statistically significant for the third and fourth quartiles compared to the reference group (first and second quartiles combined). Using the binary variable (above or below the 90th percentile), the odds ratio was below 1.0. The risk estimates for the 90th percentile and higher group did not change when excluding homes with no detectable indoor contact voltage (*n* = 270, OR = 0.83, 95% CI: 0.44, 1.58), and excluding children that lived in the house less than 12 months prior to diagnosis/ reference date ( $n = 427$ , OR = 0.78, 95% CI: 0.39, 1.54). Similarly, the risk estimates remained the same when removing the 23 non-ALL cases (OR  $= 0.82$ , 95% CI: 0.42, 1.58) or the 11 cases with Down syndrome ( $OR = 0.87, 95\%$  CI: 0.47–1.62). Multivariable analyses of  $V_{W-E}$  were similar to  $V_{bath}$  with odds ratios generally close to 1.0 or nonsignificantly below 1.0 (Table 6).

Multivariable results for indoor magnetic-field measurements indicated nonsignificant odds ratios of 1.23 (95% CI: 0.74, 2.04) and 1.18 (95% CI: 0.71, 1.96) in the highest two quartiles of exposure compared to the first quartile (Table 7). Analyses using other exposure categories, including <90th percentile as unexposed and a priori cut points, and treating the magnetic field measure as a continuous variable also indicated nonsignificantly elevated or nonsignificantly reduced odds ratios. Analyses restricted to ALL cases only, children without Down syndrome, and children residing in same home more than 12 months prior to diagnosis/reference reported similar results (not shown).

#### **DISCUSSION**

A number of studies have examined the relationship between childhood leukemia and residential magnetic fields. No epidemiological study to date has investigated contact current exposure as a possible risk factor for childhood leukemia or as a confounder for previously reported associations between residential magnetic fields and childhood leukemia. The purpose of this exploratory study was to characterize residential contact voltage in a well-defined case-control study population.

Despite the comprehensive and thorough measurement survey, no evidence was found of an association between the risk of childhood leukemia and indoor or outdoor contact voltage levels or the residential magnetic fields. Despite the weak correlations between  $B_{\text{avg}}$  and the two voltage quantities, there was nonetheless evidence of positive associations between  $B_{\text{avg}}$ and  $V_{\text{bath}}$  and  $V_{\text{W-E}}$  when the variables were organized as categorical variables (data not shown).

The study design included in-home visits and direct measurements rather than assessing exposure based on proxy measures such as the conductivity of the household pipes. The use of direct measures for contact current allows for direct statistical analyses using continuous exposure variables. Direct measures, although powerful, are limited by their ability to accurately assess true exposure. In this situation, the true exposure is strongly influenced by frequency of exposure (i.e., bathing). Unlike exposure to magnetic fields, exposure to

contact currents is intermittent. Based on the results of the pilot study, we can conclude that children do make regular contact with sources of electric current while bathing and do bathe with some regularity. However, the bathing behaviors of children in this measurement study are not known and can only be inferred from the pilot study in a comparable California population. Frequency of a child's bathing and frequency of contact with faucets were not assessed in this study to minimize participant burden.

Influences on the exposure measurements from variables such as season, time of the day, and ambient temperature were assessed and did not appear to affect the risk estimates. Although ambient temperatures in a period of a month around the exposure measurement would be preferable, both Northern and Central California have fairly stable temperatures and the 1-day measurement was considered sufficient for assessing the influence of temperature and air conditioning use at the time of measurement.

The difficulty of assessing exposure in the years preceding diagnosis is a common problem in all case-control studies. It is not clear how well contemporaneous measurements accurately characterize contact current and magnetic-field exposure in general, and it is even less clear how well they characterize past exposure (23). There was a relatively short interval between diagnosis/reference date and measurement (2.0 years for cases and 2.7 years for controls), making it more likely that the measurements are correlated with exposure in the house prior to the diagnosis/reference date. However, the residential stability inclusion criterion may have resulted in a narrower range of exposures than might exist in the overall source population.

Control subjects in the NCCLS have a higher household income compared with the cases, thereby raising some concern regarding participation bias (controls of higher socioeconomic status may be more residentially stable, easier to locate and more likely to participate). Although the analyses were adjusted for household income, there may be potential residual confounding due to undetected differences in SES between cases and controls. In addition, the residential stability criteria for this measurement study (living in same home since diagnosis/reference date) resulted in subjects with slightly higher income and education level (data not shown) than in the main study. However, household income was not correlated with any of the exposure variables, and differences in household income, Hispanic ethnicity and maternal and paternal education for participating and nonparticipating families were similar for the case and control groups. Moreover, thorough methodological analyses of the participant and nonparticipant controls in our parent study demonstrated that participating controls in NCCLS are not significantly different from first choice (participating and nonparticipating) controls with regard to demographic measures such as parental education and maternal reproductive history (24).

Although this is the first epidemiological study of contact currents and childhood leukemia, previous exposure studies have measured residential contact voltage. These studies include a pilot study of 36 residences in Pittsfield, MA (19), where the sample was weighted toward residences with proximity to high-voltage transmission lines or large three-phase primary distribution lines, a sample of 191 residences from the Denver, CO metropolitan area where 9% of residences were classified as very high current configuration but not prescreened for  $V<sub>bath</sub>$  (10), and a convenience sample of 15 homes in San Jose, CA where residences were screened for  $V_{\text{bath}} > 20$  mV (20). The median values for all three exposure metrics were substantially lower in the NCCLS population than those reported in these three exposure studies conducted with a small number of carefully selected residences in largely urban communities. For example, the largest sample, from Denver, had median values for  $V_{\text{bath}}$ ,  $V_{W-E}$  and  $B_{avg}$  of 1.0 mV, 201 mV and 0.069  $\mu$ T, respectively, compared to 0.3 mV, 83.5 mV and 0.021 μT, respectively, for the NCCLS population. This difference is likely due to

newer home construction and smaller loads on the distribution systems feeding many of the neighborhoods in the 35-county area of the California (NCCLS) study. In the Denver study, 65% of the residences were built before 1970, whereas in the NCCLS study, only 40% of the study participants resided in homes that were built prior to 1970 (decreasing the likelihood of having conductive drain-pipes). In addition, a large proportion of the homes in the NCCLS (85%) were reported to have water plumbing components, including drains, either completely or partially made of nonconductive materials.

In summary, results from our study and the three prior measurement studies demonstrate that the potential for contact current exposure in a large portion of the NCCLS study population is very low. With only 10% of the study population having magnetic-field levels over  $0.1 \mu T$  (Table 3), the potential for exposure to magnetic fields was also very limited in this population.

Based on previous studies that reported a positive relationship between residential magnetic fields and measures of contact voltage (10, 19, 25), this study was designed to address whether exposure to contact voltage was an independent risk factor for childhood leukemia or served to confound the association of magnetic fields with childhood leukemia. We did not observe a positive association between contact voltage and childhood leukemia and, because there was no association of magnetic fields with childhood leukemia in this population, the opportunity for detecting confounding was minimal. However, low exposure prevalence for both exposures limited the study's power to detect significant odds ratios for either exposure taken independently or confounding of magnetic fields by measures of contact current exposure.

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Socio-demographic Characteristics of Cases and Controls in NCCLS Contact Current Study



 $a_p$  derived from  $\chi^2$  tests for categorical variables and *t* tests for continuous variables.

Characteristics of Residential Measurements in NCCLS Contact Current Study



 $a$ <sup>*a*</sup>  $P$  derived from  $\chi^2$  tests for categorical variables and *t* tests for continuous variables.

Description of the Three Primary Exposure Variables, NCCLS Contact Current Study Description of the Three Primary Exposure Variables, NCCLS Contact Current Study



Bavg is the indoor magnetic-field measurement.

*b* Vbath is the indoor contact voltage measurement (voltage measured between the faucet and the drain in the bathtub). *c* VW-E is the outdoor contact voltage measurement (voltage measured between the water main and pole in the ground).

Correlation Coefficients*<sup>a</sup>* for Exposure Variables (log-transformed) and Study Variables, NCCLS Contact Current Study



*a* Spearman coefficients unless indicated otherwise.

*b* Bavg is the indoor magnetic-field measurement.

<sup>*c*</sup> V<sub>bth</sub> is the indoor contact voltage measurement (voltage measured between the faucet and the drain in the bathtub).

*d* VW-E is the outdoor contact voltage measurement (voltage measured between the water main and pole in the ground).

*e* Pearson coefficients.

Risk of Childhood Leukemia in Relation to Indoor Contact Voltage (V<sub>bath</sub>), NCCLS Contact Current Study



*a*<br>
All odds ratios were adjusted for household income, age, sex, Hispanic ethnicity and mother's race.

*b* Quartiles 1 and 2 were combined because 47% of observations had a zero reading.

Risk of Childhood Leukemia in Relation to Outdoor Contact Voltage (V<sub>W-E</sub>), NCCLS Contact Current Study



*a*<br>
All odds ratios were adjusted for household income, age, sex, Hispanic ethnicity and mother's race.

Risk of Childhood Leukemia in Relation to Indoor Magnetic-Field Exposures, NCCLS Contact Current Study



*a*<br>
All odds ratios were adjusted for household income, age, sex, Hispanic status and mother's race.