# Risk of Adult Acute Leukemia in Relation to Prior Immune-related Conditions[1]

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## Abstract

**We explored the association between immune-related conditions and adult acute leukemia in a study of 624 patients with acute myeloid leukemia (AML), 124 patients with acute lymphoblastic leukemia (ALL), 63 patients with other acute leukemias, and 637 healthy population controls. Common childhood viral diseases were weakly associated with AML and ALL, particularly with early exposure (≤5 years of age). Odds ratios (ORs) were elevated for chicken pox and measles at any age, but only the associations with measles were statistically significant [OR = 1.89; 95% confidence interval (CI), 1.40–2.56 for AML and OR = 1.81; 95% CI, 1.07–3.06 for ALL]. There was no association between other infectious diseases, allergies, asthma, or eczema and risk for AML or ALL, although there was a significant association between psoriasis and ALL (OR = 3.23; 95% CI, 1.25–8.30). These results offer little support for either a protective effect of enhanced immune surveillance or a harmful effect from antigenic stimulation in relation to risk for acute leukemia in adults. However, the associations between cancer risk and childhood infectious diseases are intriguing and may warrant additional research.**

## Introduction

Acute leukemias account for approximately 50% of leukemia deaths. Although ALL[3] most commonly occurs in children, AML occurs primarily in adults, with a median age at onset of 67 years (1). Exposure to radiation, benzene, alkylating agents, and smoking has been associated with the occurrence of acute leukemias, but the etiology of most cases is unknown (2).

Several hypotheses have been proposed concerning the role of immune function in the etiology of hematopoietic cancers, and some epidemiological studies have evaluated the role of immune-related medical conditions. Under the immune surveillance hypothesis, allergies, asthma, and eczema have been proposed to be protective against AML and other cancers because of an enhanced ability of the immune system to eliminate cells that have undergone malignant transformation (3). In contrast, the antigenic-stimulation hypothesis postulates that immune-stimulating conditions (including infectious diseases, allergies, and autoimmune diseases) would be associated with increased risks of lymphoblastic neoplasms due to the enhanced opportunity for malignant transformation of WBCs (4).

The extent to which either of these hypotheses holds for specific hematopoietic cancers is unclear. The role of infectious agents has been explored in relation to childhood leukemia (5) and for some forms of lymphomas (6–13). However, little information is available pertaining to acute leukemias in adults, and previous studies investigating immune-related conditions have been fairly small (100–250 cases; Refs. 3, 4, 14, and 15) or have combined chronic and acute lymphoblastic and myeloid leukemias (16). We undertook this analysis of immune-related medical history risk factors as part of a large, multiinstitutional case-control study designed to evaluate environmental risk factors for acute leukemia in adults. We examined specific diseases that have been reported in previous studies of adult hematopoietic malignancies, including common childhood viral illnesses, other viral and bacterial infectious diseases, allergies, and autoimmune diseases.

## Materials and Methods

This case-control study of risk factors for acute leukemia was conducted in collaboration with CALGB (CALGB 8661), a multiinstitutional cooperative cancer treatment group. The study was approved by the Institutional Review Boards of the NIH and of the individual participating hospitals. Details of participant recruitment and data collection have been reported previously (17).

Newly diagnosed acute leukemia patients ages 18–79 years residing in the United States or Canada who participated in any of several chemotherapy clinical trials for adults with ALL or AML sponsored by CALGB were invited to participate. After informed consent was obtained, trained interviewers contacted the patients in the hospital and either completed the telephone interview at that time or arranged an appointment. Next-of-kin interviews were arranged in situations in which the patient was too ill or had died shortly after diagnosis; 22% of the interviews were conducted solely with a proxy, and 11% were conducted jointly with the patient and a close relative.

Two groups of cases were included in the present analysis. The first recruitment period began in January 1986 and lasted

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[3] The abbreviations used are: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; OR, odds ratio; CI, confidence interval; CALGB, Cancer and Leukemia Group B.

*Table 1* Demographic distribution of AML, ALL, and other acute leukemia cases and controls

| | Cases | | | | Controls |
|---|---|---|---|---|---|
| | AML ($n$ = 624) $n$ (%) | ALL ($n$ = 124) $n$ (%) | Other[a] ($n$ = 63) $n$ (%) | Total ($n$ = 811) $n$ (%) | ($n$ = 637) $n$ (%) |
| Age (yrs) | | | | | |
| <40 | 199 (31.9) | 77 (62.1) | 26 (41.3) | 302 (37.2) | 231 (36.3) |
| 40–59 | 207 (33.2) | 27 (21.8) | 19 (30.2) | 253 (31.2) | 216 (33.9) |
| >60 | 218 (34.9) | 20 (16.1) | 18 (28.6) | 256 (31.6) | 190 (29.8) |
| Gender | | | | | |
| Female | 277 (44.4) | 39 (31.5) | 23 (36.5) | 339 (41.8) | 262 (41.1) |
| Male | 347 (55.6) | 85 (68.6) | 40 (63.5) | 472 (58.2) | 375 (58.9) |
| Race | | | | | |
| White | 536 (85.9) | 111 (89.5) | 56 (88.9) | 703 (86.7) | 547 (85.9) |
| Non-white | 86 (13.8) | 13 (10.5) | 7 (11.1) | 106 (13.1) | 89 (14.0) |
| Missing | 2 (0.3) | 0 (0.0) | 0 (0.0) | 2 (0.3) | 1 (0.2) |
| Education | | | | | |
| <High school | 160 (25.6) | 30 (24.2) | 11 (17.5) | 201 (24.8) | 129 (20.3) |
| Completed high school | 202 (32.4) | 40 (32.3) | 21 (33.3) | 263 (32.4) | 232 (36.4) |
| >High school | 234 (37.5) | 44 (35.5) | 25 (39.7) | 303 (37.4) | 236 (37.1) |
| Missing | 28 (4.5) | 10 (1.6) | 6 (9.5) | 44 (5.4) | 40 (6.3) |
| Smoked | | | | | |
| Ever | 365 (58.5) | 69 (55.6) | 30 (47.6) | 464 (57.2) | 345 (54.2) |
| Never | 240 (38.5) | 52 (41.9) | 32 (50.8) | 324 (40.0) | 273 (42.9) |
| Missing | 19 (3.0) | 3 (2.4) | 1 (1.6) | 23 (2.8) | 19 (3.0) |

[a] This category includes mixed, undifferentiated, and unclassified acute leukemias.

until January 1989 for AML cases and until June 1989 for ALL cases. Patients were classified histopathogically using French-American-British criteria; those having AML ($n$ = 434), ALL ($n$ = 124), or mixed, undifferentiated, and unclassifiable acute leukemia ($n$ = 52) identified in this recruitment phase are included in this analysis. Enrollment of AML cases was extended through September 1990. During this second recruitment period, 174 patients were categorized as AML cases, and 11 were classified as mixed leukemia cases based on French-American-British criteria. Patients with myelodysplastic syndrome were also recruited during this second period, and 16 were found to have AML after central pathological review. This brings the final sample (from both recruitment periods) to 624 AML cases, 124 ALL cases, and 63 mixed or unclassifiable acute leukemia cases. The participation rate among all eligible cases was 83% and 95% during the first and second recruitment periods, respectively.

Population-based control subjects were selected from the population by random digit dialing, and interviews were conducted from 1986 through January 1990. A total of 85% of targeted households completed a brief screening survey. Controls were frequency-matched to case subjects in the first recruitment period by sex, age (in 10-year categories), race (white or non-white), and region of residence (six regions in the United States plus Canada). The total number of identified controls was 792, and 637 (80%) of these completed the interview. Proxy interviews were required for 11% of controls, and an additional 2% of the interviews were completed with the aid of a family member.

The telephone interviews were conducted using a structured questionnaire administered by trained interviewers. The medical history section included questions about previous diagnosis of specific diseases or conditions, age at (first) occurrence, and, where appropriate, the type of medication used for the illness. Information about surgeries (tonsillectomy, adenoidectomy, and appendectomy) was also obtained.

Crude ORs and 95% CIs were calculated to assess the association between acute leukemia (total sample and separately for AML and ALL) and specific medical diseases or medical conditions. We also used logistic regression to calculate the adjusted ORs, controlling for sex, age as a continuous variable, race, education (less than high school, high school, and more than high school), and smoking status (ever and never smoked).

In the analysis of age at childhood illness, we created two groups corresponding to before school-age (≤5 years old) and older (≥6 years old). We evaluated age at onset in two ways: (*a*) we excluded participants who had not had the disease and used the older age as the reference group; and (*b*) we included everyone and used those who had not the illness as the reference group. Both methods led to similar conclusions, and the results shown are for the analysis using the full sample. We also analyzed these data using three age groups (≤5 years old, 6–10 years old, and >10 years old). There was no difference in risk between those with age of onset between 6 and 10 years and those with onset later than age 10, so those results are not presented. Because of the relatively low recall accuracy for rubella (18), we analyzed the combined childhood infectious disease history with and without the rubella question.

## Results

The demographic characteristics of the study sample are shown in Table 1. As expected from the matching procedure, controls were similar to the combined case group with respect to age, gender, and race. However, controls were slightly younger than the AML cases and older than the ALL cases (mean 47.0, 49.5, and 37.5 years for controls, AML, and ALL, respectively; $P < 0.001$).

**Association with Infectious Diseases.** The associations between a history of specific infectious diseases and the risk of acute leukemia are shown in Table 2. Patterns with respect to the common childhood viral illnesses were similar for AML and ALL, except for mumps, for which the OR was greater than 1.0 (OR = 1.23) for AML but less than 1.0 (OR = 0.68) for ALL. The adjusted OR for all acute leukemia (including mixed,

*Table 2* AML and ALL in relation to infectious disease history in 637 controls, 624 AML cases, and 124 ALL cases[a]

| | Controls | | AML | | | ALL | | |
|---|---|---|---|---|---|---|---|---|
| | No. exposed | No. not exposed | No. exposed | No. not exposed | Adjusted OR (95% CI)[b] | No. exposed | No. not exposed | Adjusted OR (95% CI)[b] |
| Childhood Viral | | | | | | | | |
| Chicken pox | 497 | 108 | 466 | 78 | 1.30 (0.93–1.82) | 102 | 12 | 1.72 (0.85–3.48) |
| Measles | 382 | 209 | 408 | 114 | 1.89 (1.40–2.56) | 69 | 37 | 1.81 (1.07–3.06) |
| Rubella | 184 | 351 | 152 | 303 | 0.93 (0.70–1.25) | 29 | 73 | 0.93 (0.55–1.59) |
| Mumps | 355 | 243 | 347 | 192 | 1.23 (0.95–1.60) | 49 | 61 | 0.68 (0.43–1.09) |
| Any[c] | 584 | 36 | 550 | 24 | 1.45 (0.82–2.56) | 117 | 3 | 3.07 (0.71–13.2) |
| Other | | | | | | | | |
| Mononucleosis | 29 | 607 | 30 | 585 | 1.22 (0.69–2.14) | 9 | 112 | 1.49 (0.64–3.44) |
| Pneumonia | 137 | 500 | 135 | 485 | 0.97 (0.73–1.29) | 22 | 102 | 0.88 (0.51–1.52) |
| Rheumatic or scarlet fever | 47 | 585 | 53 | 561 | 1.15 (0.75–1.78) | 9 | 115 | 1.48 (0.68–3.24) |
| Tuberculosis | 11 | 626 | 10 | 613 | 0.89 (0.36–2.21) | 1 | 123 | 0.70 (0.09–5.67) |
| Recurrent kidney infection | 22 | 615 | 29 | 59 | 1.20 (0.66–2.17) | 6 | 117 | 1.72 (0.65–4.60) |

[a] "Don't know" and missing responses were excluded, so the total available for analysis varies slightly among specific exposures.
[b] OR was adjusted for age (continuous), gender, race (white or non-white), education (< high school, high school, or > high school), and smoking (ever or never).
[c] Chicken pox, measles, rubella, and/or mumps.

undifferentiated, and unclassified) was suggestive of an association for chicken pox (OR = 1.33; 95% CI, 0.97–1.82) and statistically significant for measles (OR = 1.85; 95% CI, 1.41–2.45) for measles. Rubella was not associated with leukemia risk. There was little indication of a relationship with any of the other infectious diseases examined. Similar estimates were seen when the proxy respondents were excluded (data not shown). Information about vaccinations was not collected, but there was no difference in the association with measles in the younger compared to older cohorts (*e.g.*, born ≤1957 and >1957).

Risk for AML seemed to be associated with early age at onset of childhood viral infections (Table 3). An increased risk of AML for each of these infections was seen among people who reported that the illness occurred before age 6, with adjusted ORs ranging from 1.8 for younger-age chicken pox to 4.4 for younger-age measles. There was also a trend toward an elevated risk among those who reported measles at age 6 or older, (≥6 years old, OR = 1.35). When childhood illnesses were combined, the OR for AML associated with one childhood illness occurring before age 6 was less than 1.0 (OR = 0.87), but the OR increased with each additional illness for an OR = 10.1 for 4 illnesses before age 6 (trend test, $P < 0.001$). A similar pattern was seen when rubella was excluded from this analysis: OR = 0.89 (95% CI, 0.66–1.22) for 1 illness; OR = 1.67 (95% CI, 1.09–2.56) for 2 illnesses; and OR = 9.42 (95% CI, 4.78–18.6) for 3 illnesses. These relationships were not altered by adjusting for the number of siblings within the family or excluding the proxy respondents (data not shown). The risk associated with ALL in relation to early exposure to childhood illnesses was also elevated for measles (OR = 3.2; 95% CI, 1.6–6.3) and for 4 or more childhood illnesses before age 6 (OR = 5.4, 95% CI, 1.0–29.2).

**Associations with Allergic and Autoimmune Diseases.** The association between AML and ALL leukemia risk and allergies is shown in Table 4. There was no evidence supporting a protective effect of a history of specific allergies on risk for all acute leukemia combined or for AML or ALL separately, with the exception of a 2-fold increased risk (of borderline statistical significance) for ALL associated with a history of allergy to penicillin (OR = 2.15). There was no association between history of asthma, eczema, or psoriasis and risk of AML. However, there was a 3-fold increased risk for ALL associated with psoriasis.

The prevalence of most of the autoimmune disorders was low (<5% in the controls), and there was little evidence of an increased risk of AML for the specific disorders we examined (Table 4). We observed a decreased risk of AML with a history of rheumatoid arthritis (OR = 0.44), but a nonsignificant increased risk (based on only 4 cases with arthritis) for ALL (OR = 1.86, 95% CI, 0.59–5.81). An apparent association between ALL and pernicious anemia (OR = 8.27) was based on only 2 exposed cases. We repeated the analysis excluding subjects (one control, one AML case, and one ALL case) who responded "Don't know" to the question about the type of medicine used for pernicious anemia. Adjusted risk estimates were 0.45 for AML and 3.87 for ALL, and neither was statistically significant.

There was no association between history of tonsillectomy or appendectomy and AML, ALL, or all acute leukemia combined (data not shown).

## Discussion

The data from this large case-control study suggest that common childhood viral diseases, particularly at an early age of exposure, may affect the subsequent risk of adult acute leukemias. The association between AML and the number of childhood illnesses occurring before age 6 was particularly strong, with a 10-fold increase in risk for 4 or more illnesses before age 6. Although our results did not change when adjusted for

*Table 3* AML in relation to age at childhood viral illness

| | Controls *n* (%) | Cases *n* (%) | Crude OR | Adjusted OR[a] | 95% CI |
|---|---|---|---|---|---|
| Chicken pox | | | | | |
| Never | 108 (18.3) | 78 (14.4) | 1.0 | 1.0 | Referent |
| ≤5 years old | 162 (27.5) | 207 (38.3) | 1.77 | 1.81 | 1.24–2.65 |
| ≥6 years old | 320 (54.2) | 255 (47.2) | 1.10 | 1.09 | 0.76–1.55 |
| Measles | | | | | |
| Never | 209 (35.9) | 114 (22.0) | 1.0 | 1.0 | Referent |
| ≤5 years old | 71 (12.2) | 169 (32.6) | 4.36 | 4.41 | 2.97–6.55 |
| ≥6 years old | 302 (51.9) | 235 (45.4) | 1.43 | 1.35 | 0.98–1.86 |
| Rubella | | | | | |
| Never | 351 (66.9) | 303 (67.5) | 1.0 | 1.0 | Referent |
| ≤5 years old | 26 (5.0) | 48 (10.7) | 2.14 | 2.07 | 1.21–3.55 |
| ≥6 years old | 148 (28.2) | 98 (21.8) | 0.77 | 0.75 | 0.54–1.04 |
| Mumps | | | | | |
| Never | 243 (41.7) | 192 (36.1) | 1.0 | 1.0 | Referent |
| ≤5 years old | 52 (8.9) | 114 (21.4) | 2.77 | 2.72 | 1.82–4.09 |
| ≥6 years old | 288 (49.4) | 226 (42.5) | 0.99 | 1.00 | 0.76–1.32 |
| Total no. when ≤5 years old[b] | | | | | |
| 0 | 367 (62.8) | 295 (53.6) | 1.0 | 1.0 | Referent |
| 1 | 145 (24.8) | 97 (17.6) | 0.83 | 0.87 | 0.64–1.20 |
| 2 | 54 (9.3) | 62 (11.3) | 1.43 | 1.45 | 0.95–2.21 |
| 3 | 14 (2.4) | 67 (12.1) | 5.95 | 6.62 | 3.41–12.8 |
| 4 | 4 (0.7) | 29 (5.3) | 9.02 | 10.1 | 3.00–33.8 |

[a] OR was adjusted for age (continuous), gender, race (white or non-white), education (< high school, high school, or > high school), and smoking (ever or never).
[b] Analysis was restricted to participants who reported a history of at least one of these diseases, with the referent group being those for whom all reported illnesses occurred at age ≥6 years; *P* for trend test <0.001.

number of siblings, we did not have other measures to examine more directly the role of potential confounders related to birth order, socioeconomic status, or urban/rural residence during early childhood. Immune suppression is associated with an increased risk of hematopoietic and other cancers (19). The occurrence of multiple childhood illnesses at such an early age may reflect a relatively weak immune system and could be a marker of cancer susceptibility. This interpretation is speculative, however, and requires further substantiation. There have been no reports of the relationship between age of exposure to childhood infectious diseases and adult leukemia risk. Only one other study has reported data on any of these childhood illnesses and acute leukemia in adults, and the results do not support our findings. In a case-control study in China, an OR of 0.7 (95% CI, 0.4–1.2) was found for mumps and acute nonlymphocytic leukemia (236 cases), and an OR of 1.5 (95% CI, 0.7–3.0) was seen for ALL (81 cases; Ref. 15). However, mumps was relatively uncommon in the Chinese study population, with only 10% of controls reporting a positive history.

We did not see an association between other infectious diseases and acute leukemia in our study, although the power to detect an association ≤2.0 was low (<0.50) in many cases (particularly for the analysis of ALL). Three previous studies have reported data pertaining to tuberculosis history and AML, with ORs of 0.5, 0.7, and 1.4 (4, 14, 15), but there have been no other reports of the specific infectious diseases we studied in relation to the adult acute leukemias. The reported associations between other hematopoietic cancers (primarily lymphoma and multiple myeloma) and childhood viral illnesses or other infectious diseases have been inconsistent (6–13).

Our results do not support the hypothesis of a protective effect of a history of allergies or "hyperimmune" conditions such as asthma and eczema on AML risk, as has been reported in some previous studies (3, 4, 14, 15). We also saw no consistent relationship between autoimmune diseases and AML risk: only one statistically significant association (for rheumatoid arthritis) was seen (OR = 0.44), and the estimated risks for the other conditions ranged from 0.58–1.54. Previous case-control studies have also reported inconsistent findings for rheumatoid arthritis and AML (ORs ranging from 0.5–4.5; Refs. 3, 14, and 15), but increased risks for lymphoma and multiple myeloma (20–23) have been demonstrated in cohort studies of rheumatoid arthritis patients. In two of these studies, a statistically significant increased risk of leukemia (type unspecified) was seen in males but not in females (22, 23).

For ALL, we found no evidence of a protective effect of allergies. The one statistically significant association seen within this group (with penicillin allergy, OR = 2.15) could be due to chance or could reflect a potential hematopoietic effect of other antibiotics that may be used instead of penicillin by allergic individuals. The ALL risks associated with eczema, psoriasis, and rheumatoid arthritis in our study were generally elevated, but only the risk for psoriasis was statistically significant (OR = 3.23). Drugs used to treat psoriasis such as coal tar products or methotrexate, rather than psoriasis *per se*, could be responsible for any increased risk. The other autoimmune conditions we examined were very uncommon, and our power to detect small or moderate associations (OR ≤ 2.0) within the ALL group was low (<0.50).

One limitation of our study is that we relied solely on self-reported medical histories. The accuracy of reported occurrence of infectious diseases was reported in a study of ninety-five 50-year-old adults by Krall *et al.* (18). Agreement between the recalled data and prospectively collected medical records (obtained biannually from ages 1 through 10, and annually from 10 to 18) was between 70 and 80% for chicken pox, measles, and mumps, but only 34% for rubella. Agreement on age at onset was also characterized as good (>60% within 2 years), but specific data for these 3 diseases were not provided. The associations we observed with early childhood ill-

*Table 4* AML and ALL in relation to inflammatory and autoimmune diseases in 637 controls, 624 AML cases, and 124 ALL cases[a]

| | Controls | | AML | | | ALL | | |
|---|---|---|---|---|---|---|---|---|
| | No. exposed | No. not exposed | No. exposed | No. not exposed | Adjusted OR (95% CI)[b] | No. exposed | No. not exposed | Adjusted OR (95% CI)[b] |
| Allergies | | | | | | | | |
| Hay fever | 96 | 540 | 94 | 528 | 1.02 (0.74–1.42) | 23 | 99 | 1.01 (0.57–1.76) |
| Bee or wasp | 32 | 604 | 31 | 590 | 1.00 (0.59–1.68) | 5 | 117 | 0.78 (0.29–2.12) |
| Penicillin | 39 | 597 | 38 | 583 | 1.0 (0.64–1.69) | 12 | 110 | 2.15 (1.04–4.44) |
| Other | 82 | 554 | 101 | 520 | 1.24 (0.88–1.73) | 12 | 110 | 0.61 (0.30–1.25) |
| Total no. of allergies | | | | | | | | |
| 0 | 423 | – | 403 | – | 1.0 (referent) | 78 | – | 1.0 (referent) |
| 1 | 155 | – | 141 | – | 0.94 (0.71–1.24) | 28 | – | 0.92 (0.55–1.52) |
| ≥2 | 58 | – | 76 | – | 1.33 (0.90–1.95) | 15 | – | 1.10 (0.55–2.18) |
| Asthma | 54 | 583 | 38 | 584 | 0.73 (0.46–1.15) | 10 | 111 | 0.87 (0.40–1.88) |
| Eczema | 26 | 611 | 27 | 587 | 1.13 (0.62–2.04) | 9 | 114 | 1.70 (0.69–4.20) |
| Psoriasis | 19 | 617 | 27 | 593 | 1.31 (0.70–2.44) | 7 | 115 | 3.23 (1.25–8.30) |
| Rheumatoid arthritis | 26 | 608 | 14 | 604 | 0.44 (0.22–0.91) | 4 | 117 | 1.86 (0.59–5.81) |
| Other arthritis, bursitis, rheumatism | 139 | 494 | 163 | 456 | 1.09 (0.81–1.47) | 18 | 105 | 1.02 (0.54–1.93) |
| Insulin-dependent diabetes[c] | 13 | 601 | 10 | 580 | 0.67 (0.28–1.62) | 1 | 120 | 0.77 (0.10–6.20) |
| Pernicious anemia | 2 | 632 | 2 | 617 | 0.88 (0.12–6.30) | 2 | 122 | 8.27 (1.11–61.8) |
| Other[d] | 15 | 614 | 9 | 608 | 0.58 (0.25–1.34) | 2 | 121 | 0.99 (0.22–4.54) |

[a] "Don't know" and missing responses were excluded, so the total available for analysis varies slightly among specific exposures.
[b] OR was adjusted for age (continuous), gender, race (white or non-white), education (< high school, high school, or > high school), and smoking (ever or never).
[c] Non-insulin-dependent diabetes mellitus was excluded from exposed and nonexposed categories.
[d] This category includes connective tissue diseases, rheumatic heart disease, ankylosing spondylitis, and other autoimmune conditions.

nesses (<age 6) were seen when proxy respondents were excluded and when rubella was eliminated from the analysis. This provides some reassurance that our findings are not the result of misclassification bias.

Overall, we observed an association between adult acute leukemia risk and common childhood viral illnesses, particularly when these occurred at an early age. These associations should be explored in relation to other factors such as number of siblings, birth order, and factors relating to socioeconomic status in childhood to more fully understand the potential relationship between childhood illnesses and leukemia risk in adulthood.

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