

Trends in childhood acute lymphoblastic leukemia in Western Australia, 1960–2006

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Increases in the incidence of childhood acute lymphoblastic leukemia (ALL) have been reported in some countries, while other reports from similar geographical regions have indicated stable rates. The reasons for the discrepancies have been debated in the literature, with the focus on whether the observed increases are “real” or an artifact resulting from improvements in diagnosis, case ascertainment and population coverage over time. We used population-based data from Western Australia to investigate trends in the incidence of childhood ALL between 1960 and 2006. Age-standardized incidence rates (ASRs) and rate ratios (indicating annual percent change) were estimated using Poisson regression. Between 1960 and 2006, the ASR was 3.7 per 100,000 person-years, with an annual percent increase of 0.40% (95% CI: -0.20, 1.00). Between 1982 and 2006, the ASR was 3.8, with an annual percent increase of 0.80% (95% CI = -0.70 to 2.30). This increased to 1.42% (95% CI: -0.30, 3.0) when a sensitivity analysis was undertaken to assess the effect of excluding the final 2 years of data. Annual increases of 3.7% (95% CI: -0.50, 8.00) among children aged 5–14 years, and of 3.10% (95% CI: 0.50, 5.70) in girls, were observed for this latter period. These results were supported by national Australian incidence data available for 1982–2003. There may have been a small increase in the incidence of ALL since 1982 among girls and older children, but an overall increase appears unlikely. No impact of folate supplementation or fortification is apparent.

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Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, accounting for ~25% of childhood cancer diagnoses each year worldwide.¹ Despite extensive research over many years, little is known about the etiology of ALL, although a growing number of theories implicating genetic, *in utero* and environmental factors are emerging.

Research groups from the UK, Europe, the USA and New Zealand have reported increases in the incidence of childhood ALL over the last 3 to 4 decades, while other research groups from similar geographical regions have reported stable rates.² There has been considerable debate in the literature as to whether such reported increases are “real,” and possibly due to changes in environmental or demographic risk factors; or whether they represent—at least in part—artifact resulting from improvements in diagnosis, case ascertainment and population coverage over time.^{2,3} As cancer reporting is voluntary and national coverage not yet achieved in many of these countries,^{4,5} distinguishing between these possibilities is problematic.

In Australia, cancer notification has been mandatory from 1982 and population coverage and case ascertainment of the childhood leukemias are considered to be virtually complete. Furthermore, in Western Australia (WA), we have population-based incidence data on hematological malignancies from 1960.

A study published in 2001 by our colleagues reported a 60% reduction in risk of common ALL among children of WA women who took folate supplements (with or without iron) during pregnancy.⁶ Periconceptional folate supplementation for the prevention of neural tube defects has been promoted in WA since 1992. In addition, voluntary fortification of some foods (mainly breakfast cereals) has been permitted since 1996. Mandatory fortification of bread making flour with folic acid was recently approved for Australia and New Zealand (June 2007).

The aim of this study was to use population-based Western Australian data to investigate whether the rate of childhood ALL has

increased over the past 47 years. We also aimed to investigate whether the promotion of folate supplementation or voluntary fortification of foods may have influenced the incidence of ALL.

Material and methods

Sources of data on ALL cases

Case notifications were from 2 sources. Information on ALL diagnoses between 1960 and 1981 was obtained from the former Leukemia and Allied Disorders Registry (LADR) of Western Australia. Data had also been collected for 1958–59, but were omitted from our analysis because of concerns about the quality of the data during that period. Cancer notification was not mandatory at that time; however, comprehensive notification was achieved since most of the hematologists, pathologists and clinicians involved in the treatment of lympho-hematopoietic neoplasms were members of the Registry Committee and its Diagnostic Group. The Committee met monthly to collate new cases, for many of which the provisional (unreviewed) diagnosis was reviewed by an expert group. More advanced diagnostic techniques led to discontinuation of the review process after 1975.

There were 200 cases of childhood ALL identified using LADR data for the period 1960–1981; in addition, there were 20 cases recorded as “acute leukemia—not otherwise specified (NOS)” (15 of which had been reviewed by the Diagnostic Group). These NOS cases were enumerated to allow assessment of any potential effect of the level of certainty of diagnosis on changes in incidence over time (see below). Of cases diagnosed from 1960 to 1975, 86.1% had both an “unreviewed” and a “reviewed” diagnosis. Diagnostic review mainly served to classify further the “acute leukemia NOS” group by cell type. Based on the premise that the reviewed diagnosis was more likely to be correct, we used the reviewed diagnosis when it was available and the unreviewed diagnosis for the remaining cases.

Information about 341 cases of ALL diagnosed between 1982 and 2006 was provided by the population-based Western Australian Cancer Registry (WACR), which was established in 1981. There were no cases of childhood “acute leukemia NOS” recorded during this period. At the time of writing this article, the cancer data for 2006 were preliminary.

For comparison with national trends in ALL, incidence data for all of Australia—available from 1982 to 2003—were obtained from the Australian Institute for Health and Welfare (AIHW).⁷ Cancer incidence data are provided to the National Cancer Statistics Clearing House at the AIHW by all state and territory cancer registries, all of which are members of the Australasian Association of Cancer Registries (AACR). Cancer notifications to the AIHW are mandatory and all efforts are made to check for duplicate cases among contributing registries.

Abbreviations: ALL, acute lymphoblastic leukemia; WA, Western Australia; LADR, Leukemia and Allied Disorder Registry; WACR, Western Australian Cancer Registry; NOS, not otherwise specified; AIHW, Australian Institute for Health and Welfare; AACR, Australasian Association of Cancer Registries.

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