

Height and lymphoblastic leukaemia

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SUMMARY Two hundred and thirty six children with untreated lymphoblastic leukaemia were compared for height with the normal population by calculation of their mean standard deviation score. As a group, they proved to be significantly taller ($P < 0.0001$), which gives support to the theory that growth hormone or a somatomedin may be involved in the development of the disease.

The treatment of malignant diseases during childhood leads to variable growth problems which have been studied in some detail.¹ The effects on growth of the actual disease processes themselves have been relatively neglected, but in a preliminary study² the observation was made that a group of Sheffield children with untreated leukaemia were significantly taller than their healthy peers. To confirm or refute this unexpected finding the survey was extended to include children from all over the United Kingdom in a retrospective review of the multi-centre Medical Research Council (MRC) childhood leukaemia trial, UKALL II.

Methods

The MRC UKALL II trial took place between January 1972 and September 1973. Criteria for entry included all children over one year who had untreated lymphoblastic leukaemia, but for the purpose of this study boys over age 12 and girls over age 10 were excluded in order to eliminate the unpredictable effect of the pubertal growth spurt.

The height and weight of each child at the time of diagnosis was recorded by each participating centre for the purpose of drug dose calculation. The height was converted to a standard deviation (SD) score in order to eliminate the effects of age and sex.³ Normal values were obtained from the data of Tanner *et al.*⁴ For a normal population the mean SD score is 0 with an SD of 1. The data were further subdivided according to sex, and whether the child was above or below the median age for the group. Standard statistical techniques were used for analysis with Student's *t* test where appropriate.

Results

Two hundred and thirty six children, with a median

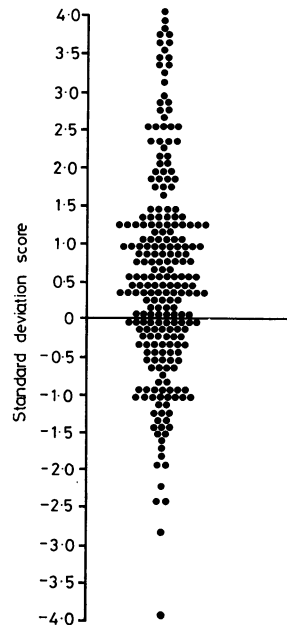


Figure Standard deviation score for height of 236 children entering the MRC Childhood Leukaemia Trial, UKALL II.

age of 4.3 years, from 26 centres scattered throughout the United Kingdom, were studied. Of these 140 were boys and 96 girls.

The group as a whole was significantly taller than the normal population ($P < 0.0001$). There was no difference between the sexes, nor was there a difference between those older and younger than the median age. Of the four subgroups (boys < 4.3 years, boys > 4.3 years, girls < 4.3 years, girls > 4.3 years), all except the boys > 4.3 years were significantly taller than normal (Table and Figure.)

Discussion

This nationwide study of a socially mixed population of children with lymphoblastic leukaemia offers confirmation of our earlier impression that

Table Standard deviation scores of height of children with leukaemia at diagnosis

	Total	Boys	Girls	<4.3 years >4.3 years		Boys		Girls	
						<4.3 years	>4.3 years	<4.3 years	>4.3 years
Number	236	140	96	117	119	72	68	45	51
Mean	0.492	0.415†	0.605†	0.638*	0.350*	0.671	0.144	0.584	0.624
SD	1.385	1.442	1.296	1.508	1.242	1.574	1.242	1.411	1.199
Significance of difference from normal population	P<0.0001	P<0.001	P<0.001	P<0.001	P<0.01	P<0.001	NS	P<0.01	P<0.001

†*No significant difference between these groups. NS=not significant.

such patients are taller, overall, than they should be. It is based on the assumption, however, that the normal values for height described by Tanner *et al.*⁴ in 1965 are still relevant to the general population of children in Britain. These data were collected during the middle to late 1950s, and to eliminate any bias due to secular trends over the 13 to 20 year gap a time matched control group would have been needed, but since this was a retrospective study this was impossible. Despite that, it is reassuring that similar recent reports using the same technique have identified groups of children both taller and shorter than normal, so on balance it seems likely that our calculations are valid.¹⁻³ Another potential bias, the effect of varying techniques in estimating height, is less likely to have influenced our results since random measurement errors in the 26 centres would have tended to cancel each other out.

Why then should children with untreated lymphoblastic leukaemia be taller than average? Rogers *et al.*⁵ have postulated that growth hormone, or a growth hormone-dependent somatomedin, may be concerned in the development of the disease; and growth hormone has been shown to have a trophic effect on lymphoid tissue.⁶ Furthermore, hypophysectomy in rats with induced T cell leukaemia can suppress the disease process,⁷ and Schedewie *et al.*⁸ have recently confirmed that growth hormone values in children with lymphoblastic leukaemia were significantly higher at diagnosis than later during remission. Surprisingly, perhaps, in their group of 127 children they could detect no increase in height, and one subgroup (boys <4 years) was apparently shorter than average.

Unfortunately, we have no information available on parental heights and cannot determine whether our children are taller than might be predicted. This means that we do not know at present whether leukaemia occurs in constitutionally tall children or whether there is some acquired aberration of growth associated with the disease.

It should be noted that the clinical effect of the extra length in any individual would be negligible. One SD for height is only 6.65 cm for an 18 year old boy or 6.0 cm for a 16 year old girl, so the extra height of these children at diagnosis is similar in magnitude to the potential loss in ultimate height as a result of irradiation of the central nervous system.¹

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