

# Impaired Pubertal Growth in Acute Lymphoblastic Leukaemia

This extensive, long-term study of 182 children surviving acute lymphoblastic leukemia (ALL) focuses on their growth at the Hospital for Sick Children in London. The children were in first remission, had been off treatment for 2 years or more, and had attained the onset of puberty at the time of the study.

All had received cranial irradiation, usually given within 8 weeks of diagnosis: 2,400 cGy in 93 patients (before 1980, group A), and 1,800 cGy in the 89 others (group B). None had received spinal or gonadal irradiation. All patients were treated with standard chemotherapy, including intrathecal methotrexate in similar dosage regimens in either group. Mean  $\pm$  standard deviation (SD) age at diagnosis or start of treatment was  $4.8 \pm 2.6$  years in group A and  $6.5 \pm 3.3$  years in group B. Patients who received growth hormone and/or an analogue of gonadotropin-releasing hormone were not included in the study, nor were those having dysmorphic syndromes or an abnormal karyotype.

Mean height at diagnosis or start of treatment was  $-0.29$  standard deviation score (SDS) in group A, and  $+0.40$  in group B. Mean final height was  $-0.63$  SDS in group A, and  $-0.53$  SDS in group B, the number of patients having reached final height being larger in group A (44 boys and 33 girls) than in group B (16 boys and 18 girls); the differences were not significant. There was a similar reduction in height SDS for age in both groups during the time of pubertal growth spurt, more important in girls (42 in group A, 47 in group B) than in boys, and also in patients treated before age 7 years than after this age.

The effect of cranial irradiation on the age at onset of puberty was studied in children treated not later than age 7 years. In group A, puberty started at  $12.2 \pm 1.0$  years in boys and  $10.6 \pm 1.0$  years in girls. In group B, surprisingly, it started significantly earlier;  $11.4 \pm 1.5$  years in males and  $9.9 \pm 0.9$  years in females ( $P < 0.01$ ).

Uruena M, Stanhope R, Chessells JM, Leiper AD. *Arch Dis Child* 1991;66:1403-1407.

**Editor's comment:** *This long-term study of children who had undergone cranial irradiation for ALL is not the first but probably the most reliable, since the series of patients is particularly homogeneous, and the methodology for evaluation of growth and puberty particularly accurate. The results differ in some points from those reported in other series of cases. Without discussing these differences, we agree with the authors on their main conclusions, which are that: (1) a dose of 1,800 cGy impairs future growth as much as a dosage level of 2,400 cGy; (2) young age at irradiation is an important factor for later growth insufficiency; and (3) the severe impairment of final height in girls treated at less than 7 years of age probably results from a combination of growth hormone insufficiency and earlier puberty.*

*These authors did not evaluate the possible effect or role of chemotherapy, which may play an adjunctive role to irradiation in producing growth retardation, as alluded to by Dr. Shalet in his article appearing in this issue.*

*Since patients who received hormonal treatment were excluded from the study, we await data on the long-term results obtained with growth hormone therapy in the follow-up and care of the survivors of childhood ALL, and then to comparison of their natural history as analyzed by the present study.*

Jean-Claude Job, MD

**2nd Editor's comment:** *The data in this abstract, and Dr. Job's comments, complement the presentation by Dr. Shalet carried as one of the lead articles in this issue. Age, sex, chemotherapy, and irradiation dose are variables that probably help determine the ultimate height of children treated for ALL with irradiation. Rereading the section regarding ALL in Dr. Shalet's article may be useful.*

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