

Fortunately, the creation of the Genentech Foundation for Growth and Development has made it possible for several psychological studies to be initiated. These will be reported subsequently regarding the psychological importance of a possible modest gain in height among such patients as reported here. Unfortunately, these studies will not be reported for another 2 to 3 years.

Robert M. Blizzard, MD

2nd Editor's comment: This interesting report provides very good data regarding the use of GH for the treatment of children with ISS. Although these children showed an increase in final adult height, they did not exhibit a major improvement even after 10 years of GH therapy. The advantage of 2 or 3 inches gain in final height has to be correlated with the cost and the long-term duration of treatment needed to achieve such a modest gain. However, we now have clear data to present and to discuss with those patients and their families when evaluating the need for GH treatment.

Fima Lifshitz, MD

Table 2
Change in Final Height in ISS Treated With GH Compared With the Change in 2 Untreated Control Groups (cm)

	Boys	Girls
	Mean (95% CI)	
△Ht: ISS treated with GH (48 boys, 21 girls)	5.0 (3.6 to 6.3)	5.9 (3.7 to 8.1)
△Ht: ISS treated with GH minus △Ht: controls (Ht SDS <-1)	6.7 (3.7 to 9.6)	2.3 (-0.6 to 5.1)
△Ht: ISS treated with GH minus △Ht: controls (Ht SDS <-2)	9.2 (5.5 to 12.8)	5.7 (2.1 to 9.4)
Ht = height △Ht = final height minus initial predicted adult height		

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A Study of Females With Deletions of the Short Arm of the X Chromosome

A clinical and molecular study of 25 females with deletions of the short arm of the X chromosome was undertaken. The deletion breakpoints, the parental origin, and the activation status of the deleted X chromosomes were determined.

The short stature observed in Turner syndrome (TS) and in patients with terminal Xp deletions results from the deletion of a homeobox gene, *SHOX*, which escapes X-inactivation and is located in the pseudoautosomal region of Xp. In determining parental origin of the X chromosome with deletions, the paternal X chromosome was defective in the vast majority. Parental disomy of the X chromosomes was excluded in 24 of the 25 deleted X chromosomes.

In all cases where the breakpoint was in or proximal to Xp22.1, the deleted X was late replicating in all cells observed.

Of the 25 patients, 23 had short stature resulting from the deletion of the *SHOX* gene in the pseudoautosomal region of Xp. None of the patients in this study had a webbed neck, which is lymphomatous in origin, although 49% of 45,X individuals in a recent review (Ogata and Matsuo. *Human Genetics* 1995;95:607-629) had neck webbing. The studies suggest that a gene (or genes) responsible may reside on Xq or very proximal on Xp. Six of 18 patients examined were found to have a low hairline posteriorly. The most distal breakpoint in such a patient was Xp22.31. Congenital edema of the extremities was described in 2 cases with breakpoints in Xp22.3 but not in any of the other cases, even when breakpoints occurred in the very proximal part of Xp. None of the patients with breakpoints distal to Xp11 had any cardiovascular problems; however, breakpoints in or proximal to Xp11 were sometimes associated with aortic valve abnormalities.

The authors concluded that the apparently normal ovarian function seen in 2 cases of females with a single copy of the *DFFRX* gene suggests that the ovarian failure seen in cases of 45,X TS may result from a mechanism other than haploinsufficiency of *DFFRX*. The absence of neck webbing in any of the patients studied suggests that the gene for this feature may lie on Xq or very proximal Xp. There were no consensus breakpoints for the other stigmata associated with lymphatic abnormalities, skeletal abnormalities, or cardiac and renal abnormalities. The presence of excess melanocytic nevi is associated with breakpoints proximal to Xp22. There is some evidence for the presence of a gene for some of the soft features of TS, located in Xp22.3, and subject to X-inactivation. In cases of distal terminal deletions, the deleted X may remain active in a proportion of cells, resulting in a Turner-like phenotype, dependent on the degree of mosaicism and the tissue specificity.

James RS, et al. *Hum Genet* 1998;102:507-516.

Editor's comment: This presentation of a very detailed clinical and cytogenetic study contributes significantly to a better understanding of the locations of the genes on the X chromosome. We have come a long way since Ferguson-Smith determined in 1965 that deletions of the whole short arm of the X chromosome in females are associated with short stature, gonadal dysgenesis, and the classic stigmata of TS. However, 34 years have passed since then. With our ever-advancing technology, probably we will know the complete genome in the next decade. We then will understand many more intricacies of gene interaction, and the time interval to learn all this will be short.

Robert M. Blizzard, MD