

Growth Hormone Gene Deficiency: Hot Spots for Growth Hormone Gene Deletions in Homologous Regions Outside of Alu Repeats

Most types of growth hormone deficiency (GHD) do not involve the growth hormone gene, but there is a rare familial type of GHD, type 1A, that is caused by deletion of the growth hormone N gene on each chromosome 17 in affected individuals. The authors examined the specific mutation in 10 patients with type 1A GHD. These patients represented different geographic origins. Different size deletions were found in each family. The deletions appear to be related to abnormal pairing in the areas that flank the growth hormone gene, which leads to abnormal cross-overs. These areas have many Alu repeats. Since these are areas of recombination, it is possible to mismatch if there are different numbers of Alu repeats on the chromosomes inherited from mother and father. The mismatch of Alu repeats appears to make for hot spots of abnormal recombination. The areas of Alu repeats are clearly important areas for producing deletions that result in GHD since all the patients studied have this kind of mismatch deletion.

Vnencak-Jones CL, et al.
Science 1990;450:1745-1748.

Editor's comment: *Type 1A GHD is quite rare and presents a problem to the clinician in that when growth hormone is given, antibodies to it usually develop. Nevertheless, the study of these families has led to a better understanding of how mutations occur, at least in the case of the growth hormone gene. It*

appears that they are likely to occur because of mismatching of the chromosome areas outside the gene. The study is particularly important for understanding what leads to mutations of this type.

Judith G. Hall, MD

Adult Height in Boys and Girls With Untreated Short Stature and Constitutional Delay of Growth and Puberty: Accuracy of 5 Different Methods

The height predictions of 5 methods were compared with ultimate adult height in 37 boys and 32 girls with short stature associated with constitutional delay of growth and puberty (CDGP). The boys were seen initially at a chronologic age (CA) of 14.8 ± 1.7 years and the girls at 12.9 ± 2.6 years. The groups were seen ultimately at 23.1 years and 21.1 years.

For boys, the adult height was overestimated by calculation of the target height, as compared with the ultimate height, by 1.7 ± 5.7 cm. The overestimate for girls by the target height method

was 0.65 ± 4.31 cm. The Roche-Wainer-Thissen (RWT) method was the most accurate predictor for boys, underestimating the adult height by 0.53 ± 4.37 cm. In girls, the RWT method was less accurate as it overestimated the adult height by 2.6 ± 3.2 cm. The Bayley-Pinneau (BP) method overestimated significantly the ultimate height for boys (3.1 ± 5.5 cm) and underestimated the height for girls (0.8 ± 3.6 cm). The TW2 method underestimated significantly for both boys (1.76 ± 3.27 cm) and girls (4.17 ± 5.35 cm). The TW1 method was even less

predictable. In girls, all prediction methods gave similar results, with no method being significantly superior to the others. In boys, the RWT method offered the best estimates of adult height.

In the studies reported here in patients with CDGP, the adult height by the BP method was overestimated by 3.1 cm, which compares with the data in other series by this method (overestimations of 2 to 4 cm). The authors conclude that patients with CDGP usually reach an adult height in the lower normal range. The adult height of patients with CDGP is below the target height and does not reach

the height standard deviation score (SDS) for bone age observed at the initial visit.

Bramswig JH, et al. *J Pediatr* 1990;117:886-891.

Editor's comment: *The observed discrepancies of overestimations and underestimations of each method may relate to the particular ethnic group evaluated; thus, obtaining data for a particular center and the ethnic group(s) served by that center may be important in determining accurate predictions. Nevertheless, this is an*

important paper that demonstrates the variability of 5 different methods of height prediction within 1 clinic population for boys and girls with CDGP. These data do not necessarily apply to children who do not have CDGP. Particularly impressive in the data presented are the large measurements related to SDS. It is important for both clinicians and investigators who use height predictions to evaluate growth promoting therapy to know the tendency of each method to underestimate or overestimate adult height.

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