

withdrawal has not been studied. It would be of interest to repeat these studies periodically over several years before concluding that there are no permanent changes associated with the

initiation and subsequent withdrawal of rhGH in normal short children.

William L. Clarke, MD

Quality of Life of Young Adults With Idiopathic Short Stature: Effect of Growth Hormone Treatment

The authors assess the quality of life (QOL) and well-being of 89 fully grown, young adults with idiopathic short stature (ISS), some of whom had been treated with recombinant human growth hormone (rhGH) (N=24, 16 males; 0.2 to 0.3 mg/kg/wk for 3.8 to 8.1 years) and others who had not (N=65, 40 males). They also compared the data for these subjects with data for the average Dutch population of similar age. The mean adult height for all ISS children was -2.35 SD. Except for a decrease in the number of rhGH-treated subjects with a partner, there was no difference between the rhGH-treated and nontreated subjects with ISS in educational attainment, state of general health, personality inventory, or psychosocial/employment difficulties encountered because of short stature. The adult heights of the 2 populations were similar. The rhGH-treated subjects achieved an adult stature that was 3.3 cm greater than the pretreatment predicted adult height (range, -9.9 to +13.4 cm); interestingly, the rhGH-treated individuals estimated their adult height to be 13 cm (range, 0 to 28 cm) greater than they would have reached without rhGH administration, a perception also shared by their parents. Although expressing a desire to be taller, when the rhGH-treated and nontreated ISS subjects were asked if they were willing to risk loss of longevity in order to achieve greater stature by taking a lifelong medication, or to risk loss of life by a height-increasing surgical procedure, only a minority (11% to 22%) indicated a willingness to do so. Most ISS subjects were satisfied with their heights. In comparison to the general

Dutch population, there were no meaningful differences in QOL of the ISS subjects, whether treated with rhGH or not (see Table). The significance of the lower frequency of a partner in the rhGH-treated ISS subjects was unclear but not considered significant as it did not differ from the general Dutch population. The authors concluded that "the QOL of rhGH-treated and untreated young adults with ISS was similar and equal to the general population."

Rekers-Momberg LTM, et al. *Acta Paediatr* 1998;87:865-870.

Editor's comment: These data indicate that: (1) subjects with ISS do not differ from taller peers in their QOL; (2) administration of rhGH does not meaningfully increase adult stature or improve the QOL of treated subjects; and (3) the perception of the effectiveness of rhGH in increasing height is vastly overestimated by the treated subjects and their families. In the experience of this physician, it is the concern of the parents rather than of the child who has been brought with ISS for pediatric endocrine consultation. It is essential that the pediatric endocrinologist confronted with the normal child with ISS fully inform the family about the limited expectations of therapy with rhGH on adult stature and future well-being, and emphasize the greater likelihood that the child's stature will have minimal impact on his function as an adult.

Allen W. Root, MD

The Mean (SD) Values for Dimensions of the Dutch Restricted Version of the Minnesota Multiphasic Personality Inventory (NVM) for rhGH-Treated and Control Children With Idiopathic Short Stature (ISS)

Dimension of the NVM	Treated ISS (n = 17)	Controls ISS (n = 47)	Standard Population (n = 809)
Negativism	17.9 (10.3)	15.7 (9.7)	14.7 (7.7)
Somatization	5.9 (6.6)	4.7 (4.4)	5.3 (5.3)
Shyness	8.6 (7.5)	9.6 (7.6)	8.0 (6.4)
Severe psychopathology	3.1 (2.4)	2.7 (3.5)	2.7 (2.7)
Extroversion	20.4 (5.1)	19.7 (4.8)	17.1 (5.3)

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Final Height After Combined Growth Hormone and Gonadotropin-Releasing Hormone Analogue Therapy in Short Healthy Children Entering Into Normally Timed Puberty

Controversy continues as to the feasibility of using gonadotropin-releasing hormone analogues (GnRHa) in combination with recombinant human growth hormone (rhGH)

to increase final height by delaying puberty and slowing bone maturation in short non-growth hormone-deficient (GHD) children. Lanes and Gunczler evaluated the effect of 2¹/₂ years of

combined rhGH and GnRHa therapy in 10 short children (7 girls, 3 boys) with a mean chronologic age of 11.8 ± 1.2 years, mean bone age of 11.2 ± 0.9 years, and mean height -2.4 ± 0.4 SD below the 50th percentile. These children had an initial mean predicted height of 150.7 ± 9.8 cm (target height, 160.7 ± 5.3 cm) and all were in Tanner stage-II puberty. The control group included 7 girls and 3 boys with a mean chronologic age of 11.4 ± 1.0 years, mean bone age of 11.0 ± 0.8 years, and mean height -2.3 ± 0.4 SD below the 50th percentile who were in Tanner stage-II puberty. They had a mean predicted height of 151.8 ± 10.1 cm (target height, 159.5 ± 5.1 cm). No subject had GHD as determined by responses to clonidine stimulation. The subjects in the study group received rhGH at a dose of 0.1 U/kg/d SC 6 days a week (0.2 mg/kg/wk) and GnRH (leuprolide acetate) at a dose of 0.3 mg/kg IM q28d. Subjects were treated for 30 ± 5.2 months.

As anticipated, combined therapy resulted in interruption of pubertal development. Growth velocity decreased from 6.5 ± 1.6 cm/y to 3.9 ± 1.3 cm/y during the second year of combined therapy, resulting in a height z-score reduction from -2.4 ± 0.4 to -2.6 ± 0.7 SD (see Figure). Bone age maturation declined as well, averaging 0.5 bone age year/year of treatment. Predicted final height improved slightly by 12 months, but at the end of treatment was similar to baseline. The predicted final height of the study population after 2 years of therapy was 150 ± 8.0 cm while that of the control population was 151.2 ± 9.4 cm. After the discontinuation of combined therapy, growth velocity did not improve but the bone age advanced more rapidly, averaging 2.0 ± 0.4 cm/y of follow-up. The mean final height of the study group was 151.7 ± 2.4 cm, not greater than the mean pretreatment predicted final height of 150.7 ± 9.8 .

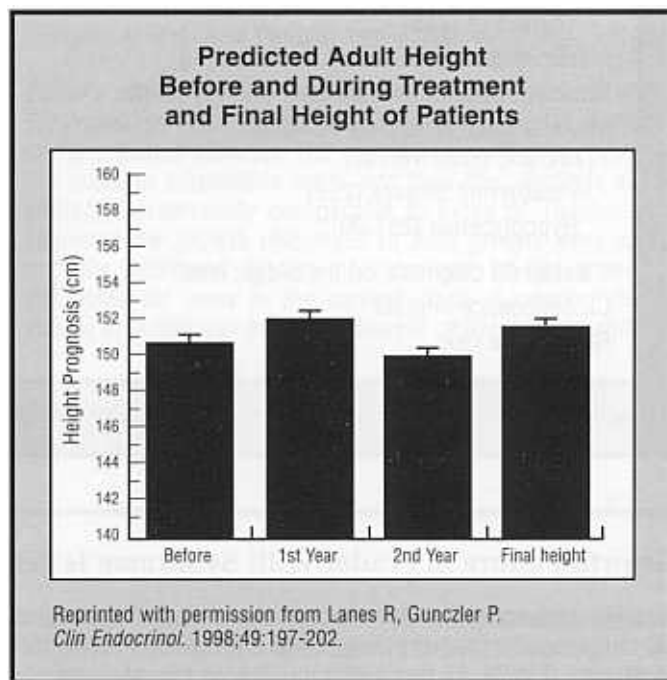
Lanes R, Gunczler P. *Clin Endocrinol* 1998;49:197-202.

Editor's comment: Although this is a study of a relatively small number of subjects, the inclusion of a very well-defined control group strengthens the findings. In this particular study, it is very clear that the combined use of rhGH and GnRHa did not increase final adult height. Whether initiating therapy in children

in slightly earlier stages of puberty or administering larger doses of rhGH might have resulted in a better outcome remains to be seen. The authors point out that this is only the second study that they know of following children receiving combined therapy to final height. The other study was conducted by Balducci and colleagues. The findings by Balducci's group produced similar results as reported by Lanes and Gunczler. These findings are important and should caution pediatric endocrinologists to be conservative in suggesting that such therapy may be of benefit to non-GHD short children who are entering puberty. Previously, several studies using GnRH alone were equally none productive.

William L. Clarke, MD

Balducci L, et al. *J Clin Endocrinol Metab* 1998;80:3596-3600.



Morbidity in Turner Syndrome

This is a report using data from the Danish Cytogenetic Central Register and the Danish National Registry of Patients to assess the morbidity of women with Turner syndrome (TS) during the 10 years from January 1, 1984, to December 31, 1993. This study includes all women living in Denmark during that period. Five hundred ninety-four women with TS were identified. The observed number of diagnoses among TS patients was compared with the expected number calculated from the incidence in the study base. Not surprisingly, the relative risk of having an endocrine diagnosis, particularly hypothyroidism and thyroiditis, was much greater in women with TS than in the general female population (see Table). Insulin-dependent and noninsulin-dependent diabetes also were increased. Congenital malformations were most consistent among patients with 45,X karyotype. Osteoporosis and fractures occurred more

frequently in women with TS, especially in the metacarpal bones and in the femoral neck. Fractures of the spine, ulna, and radius also were seen more frequently. The relative risk of cancer among women with TS does not seem to be elevated compared with the general population, except for cancer of the rectum and colon. In addition, women with TS had a significantly increased relative risk of heart disease, arteriosclerosis, hypertension, and vascular disease of the brain. Finally, the relative risk of cirrhosis of the liver was significantly elevated. As expected, the relative risk of endocrine diseases reached a maximum in the young age groups, while the relative risk of fractures reached a maximum in the older age group. The authors stress that women with TS have a risk profile similar to that of postmenopausal women.

Gravholt C, et al. *J Clin Epidemiol* 1998;51:147-158.