

in 7, and between the 10th and 50th in 8. No correlation was observed between final height and glycosylated hemoglobin concentrations, early microangiopathic complications, or thyroiditis.

The authors conclude that there was no growth retardation in their patients, that final height exceeded target genetic height, and that diabetes by itself did not impair final height.

d'Annunzio G, et al. *Diabetes Res Clin Pract* 1994;24:187-193.

Editor's comment: These 2 papers from Germany and Italy present similar findings. The data are both welcome and reassuring. Although the literature is replete with descriptions of height at diagnosis of children with diabetes, and examples of poor growth associated with extremely poor glucose control, there have been few data regarding final height in these children. The findings, however, are probably not surprising to those who care for young adults with IDDM, for short stature is not a term frequently used to characterize the adult who has had IDDM as a child.

What both of these papers fail to clarify is how one is to interpret the array of data currently published with regard to growth parameters in the diabetic child, ie, growth velocity, integrated growth hormone concentration, pulse amplitudes and frequencies, insulin-like growth factor (IGF)-1, IGF-binding protein 3, growth hormone-binding protein, and IGF-binding protein 1. What is the clinical and pathophysiologic significance of these data if the majority of diabetic children reach or exceed their predicted final adult height? Perhaps this question is best posed to the researchers currently publishing these data. Are their patients destined to have short stature, or like the patients of Holl et al, will they eventually regain their growth potential despite early decreased linear growth velocity? Long-term studies of the patients reported in previous studies are very much needed.

William L. Clarke, MD

Preliminary Localization of a Gene for Autosomal Dominant Hypoparathyroidism to Chromosome 3q13

In a kindred in which 7/15 members over 3 generations had mild, generally asymptomatic hypocalcemia associated with hyperphosphatemia and low or inappropriately normal concentrations of parathyroid hormone, linkage to chromosome 3q13 was established. This region of chromosome 3q is near that for the parathyroid cell Ca^{++} -sensing membrane receptor mapped to chromosome 3q2 (Brown et al and Pollak et al). The investigators suggest that a mechanism opposite to that identified in patients with familial hypocalciuric hypercalcemia, in which the sensitivity of the receptor for Ca^{++} is decreased or downregulated, is operative in the present family. This would mean that receptor sensitivity is upregulated and, therefore, lower concentrations of Ca^{++} are required to depress the secretion of parathyroid hormone.

Finegold DN, et al. *Pediatr Res* 1994;36:414-417.

Brown EM, et al. *Nature* 1993;366:575-580.

Pollak MR, et al. *Cell* 1993;75:1297-1303.

Editor's comment: This report illustrates yet another possible mechanism for familial hypoparathyroidism, in addition to abnormalities within the gene for parathyroid hormone itself (chromosome 11p15), which is transmitted as an autosomal recessive characteristic, and embryonic dysgenesis of the parathyroid gland, which is inherited as an X-linked recessive trait. One awaits analysis of the gene for the Ca^{++} -sensing receptor in this family and its expressed characteristics.

Allen W. Root, MD

Growth Hormone Releasing Activity by Intranasal Administration of a Synthetic Hexapeptide (Hexarelin)

This study was designed to compare the effects of intranasal versus intravenous growth hormone (GH)-releasing peptide (the hexapeptide, His-D-2-methyl-Trp-Ala-Trp-D-Phe-Lys-NH₂, known as hexarelin). Ten children with familial short stature and 2 young adults with GH deficiency were tested. The children with familial short stature had normal GH responses to clonidine and insulin, whereas the GH-deficient subjects failed to show responses to either. The GH-deficient subjects were studied after they had been off human GH for at least several years.

Each subject was given hexarelin twice within 1 week, either intravenously (IV) (1 μ g/kg) or intranasally (IN) (20 μ g/kg) initially. Blood samples for GH, thyrotropin (TSH), free thyroxine (fT_4), and triiodothyronine (T_3) concentrations were obtained at 0, 15, 30, 60, 90, and 120 minutes.

There were no differences in the mean peak GH response to hexarelin administration depending on its route of administration (79.6 \pm 53.1 mU/l IV versus 72.2 \pm 35.5 mU/l IN). However, the peak GH concentration occurred approximately 15 to 30 minutes after IV administration, while the peak GH concentration after IN hexarelin occurred 30 to 60 minutes after administration. TSH concentrations fell significantly by 120 minutes, but remained within the normal range. This fall in plasma TSH

following hexarelin administration may be the result of partial action on the hypothalamus. There were no significant changes in plasma fT_4 or T_3 . The authors conclude that this particular hexapeptide is effective as a provocative test for GH secretion.

Laron Z, et al. *Clin Endocrinol* 1994;41:539-541.

Editor's comment: This is a short but important report. GH-releasing peptides (GHRPs) are now being studied for their activity in human subjects. Although the authors of this report suggest that IN hexapeptide would be a good provocative test for GH secretion, the obvious inference is that this compound or a similar synthesized GHRP may someday be useful in treating individuals with defects in GH secretion. Demonstrating that the IN route of administration induces similar GH release as does IV administration strengthens the practicality of these compounds for use in children with GHRP-treatable disorders. The effects of chronic GHRP administration on thyroid function, however, would need to be carefully monitored based on the TSH-lowering effects of hexarelin in the present study.

William L. Clarke, MD