

Neurosecretory Dysfunction: A Treatable Cause of Short Stature

Studies presented in this article indicate that there is a group of short children who, although not growth hormone (GH) deficient by classic definition, do not secrete an adequate amount of GH during a 24-hour period to grow normally. Seven children (7.4 to 15.5 years of age) so classified met criteria consistent with GH deficiency: height less than first percentile, growth velocity <4 cm/yr, bone age at least 2 years behind chronological age, and low somatomedin-C concentrations for age, except that there was a GH peak >10 ng/ml to provocative testing. These children are classified as children with neurosecretory dysfunction (NSD). Twenty-four-hour integrated concentrations of GH (ICGH) (samples withdrawn every 20 minutes) were compared with concentrations from 16 GH-deficient children and 22 controls.

All children with NSD had nocturnal GH peaks of 10 ng/ml or greater. Six of the 16 GH-deficient patients also had nocturnal peaks of 10 ng/ml or greater. These data indicate the poor correlation between pharmacologic testing and nocturnal peaks of GH in GH-deficient children and the poor correlation between pharmacologic testing, nocturnal peaks, and ICGH in children with NSD.

	N	ICGH	No. of peaks/24 h	Area under curve	Mean per amplitude
Controls	7	5.4 ± 0.5 ng/ml	6.4 ± 0.3	129 ± 14 U	17.0 ± 1.4
GH deficient	16	1.6 ± 0.2 ng/ml	1.9 ± 0.5	26 ± 6 U	9.0 ± 2.2
NSD	22	2.1 ± 0.3 ng/ml	3.9 ± 0.6	42 ± 5 U	9.3 ± 1.2

Six of the seven patients with NSD responded to GH treatment (0.07 U/kg body weight three times weekly) nearly as well as the GH-deficient patients (a mean change in growth rate of 4.1 v 5.4 cm/yr).

In addition, the authors observed that nocturnal GH peaks in many of the children who manifested these peaks occurred in all stages of sleep except stage 4. In fact, the nocturnal GH peak may occur during another stage of sleep or in a subsequent period of stage 3 or 4. Interestingly, these investigators also found no differences in ICGH or patterns of GH secretion in children of various Tanner stages of sexual development. This is in accord with previous studies of some investigators (Thompson et al: *JCE&M* 1972;35:334), but not in accord with studies by Howse et al (*Clin Endocrinol* 1977;6:347), who suggested a pubertal increase in GH secretion based on five-hour nocturnal sampling in several short children.

As a result of these observations, the authors suggest that there is a spectrum of GH neurosecretory abnormalities ranging from absolute deficiency to a problem in GH regu-

lation not readily identified with provocative testing. They also suggest that these abnormalities are manifested by reduced number and/or amplitude of pulses, not readily identifiable with GH-stimulation tests, and that a majority of these patients respond to GH therapy with significant and sustained growth.

Spiliotis BE, August GP, Hung W, et al: *JAMA* 1984;251:2223.

Editor's comment—Spiliotis et al have demonstrated convincingly the points made in their report. It is apparent that not all patients with GH deficiency can be demonstrated by utilizing pharmacologic testing for GH release. The dilemma regarding the criteria for diagnosis of GH deficiency is emphasized from the data presented. Although the ideal method of diagnosis is to perform integrated concentrations of GH over 24 hours, this is impractical except in the research setting. These data emphasize the fact that it is difficult to determine the incidence of GH deficiency because it depends upon the criteria used to make the diagnosis.

Precocious Puberty After Hypothalamic and Pituitary Irradiation in Young Children

R. Brauner and co-workers at the Hôpital des Enfants-Malades in Paris report that six of 29 children treated with irradiation before seven years of age for medulloblastoma or other head and neck tumors, or for acute lymphoblastic leukemia, developed precocious puberty. Most developed precocious puberty within 30 months of irradiation therapy. Five had associated growth hormone (GH) deficiency. This combination of sexual precocity and GH deficiency produces short stature (136.7 cm, 143.5 cm, and 145 cm in the three patients whose heights were reported) in adult-

hood. It is important to consider that such children are at high risk for having very short adult stature, and require specific treatment of precocious puberty combined with GH therapy when a deficiency of this hormone is demonstrated.

Brauner R, Czernichow P, Rappaport R: *N Eng J Med* 1984;311:920.

Editor's comment—More and more children with tumors are surviving following irradiation therapy. This will increase the incidence of organic hypopituitarism and increase

the use of GH as a therapeutic agent. Studies using luteinizing-hormone-releasing-hormone analogue in conjunction with human growth hormone are being conducted at the University of Virginia, Boston Children's Hospital, Massachusetts General Hospital, and the University of California, San Francisco, by R.M. Blizzard, J. Crigler, J. Crawford, and S. Kaplan, respectively. Physicians who encounter patients with GH deficiency accompanied by normal adolescent sexual development, and who are going to be unacceptably short, are urged to contact these investigators.