

## Psychosocial Growth Failure: A Positive Response to Growth Hormone and Placebo

Boulton et al report their study of a double-blind placebo crossover trial of growth hormone (GH) in 7 children (3 males, 4 females, ages 3.6 to 11.6 years; bone age range of 2 to 9.5 years) with the diagnosis of psychosocial growth failure. Six of these children had a disorder of attachment dating from infancy with recurrent depression in 3. The other child had reactive depression from current family stress. All children were measured with a Harpenden stadiometer. Growth velocity and weight were converted to standard deviation scores (SDS). All children had heights <3rd percentile (-2 SDS), growth velocity <25th percentile (-0.09 SDS), and had been monitored at least 1 year at 3-month intervals. All were prepubertal at the start of the trial. GH secretion was measured at 20-minute intervals during the first 3 hours of sleep and the results analyzed using the PULSAR program. Dietary intake was assessed by computer analysis of 4-day food diaries.

Mean GH concentration during sleep was  $10.9 \pm 4.4$  mU/L with a mean peak level of  $19.6 \pm 6.7$  mU/L. All subjects had a maximum peak of 20 mU/L or greater. Mean peak interval was  $147 \pm 108$  minutes. The mean ( $\pm$  SEM) insulin-like growth factor 1 (IGF-1) was  $1.08 \pm 0.31$  U/mL. The mean ( $\pm$  SEM) SDS growth velocity prior to treatment was  $-2.32 \pm 0.122$ , for the placebo period  $-0.6 \pm 0.69$ , and for the GH treatment period  $+4.66 \pm 1.88$ . Significant differences in velocity between each of the 3 periods were demonstrated by analysis of variance ( $P < 0.0001$ ). The greatest difference between growth velocities was between the pretrial and GH periods ( $P < 0.001$ ). The order of treatment did not affect the growth response. The mean ( $\pm$  SEM) IGF-1 did not change significantly during GH treatment ( $1.24 \pm 0.34$  U/mL at the end of treatment versus  $1.09 \pm 0.31$  U/mL pretreatment). The mean daily food energy intake was similar for the trial, pretrial, and posttrial periods.

Boulton TJC, Smith R, Single T. *Acta Paediatr* 1992;81:322-325.

**Editor's comment:** This is an interesting report, but it is not clear that the children studied had classic psychosocial dwarfism. While in their adverse environment, as defined by Powell et al, children with this syndrome often have reversible GH deficiency with abnormal GH responses to pharmacologic stimuli. GH secretion in the children in the present study was normal. Therefore, they were not shown to have GH secretory dysfunction. The authors acknowledge this, and suggest that the GH secretion and growth response of these children are similar to those of children with constitutional delay of growth.

*However, the presence of a significant placebo effect suggests that the intervention may have altered family dynamics in some manner. Even though these children do not necessarily fit the original criteria for the definition of psychosocial dwarfism, they clearly had psychological dysfunction and significant growth retardation that responded to GH administration. Thus, these children, and other similar children, may be potential candidates for GH treatment. Whether or not such treatment may alter their psychological status is left for speculation.*

William L. Clarke, MD

**2nd Editor's comment:** The topic of psychosocial short stature (PSS) has been of great interest since we (Powell et al, *N Engl J Med* 1967) reported a group of children with the syndrome who had reversible hyposomatotropism. Recently, I have written 2 reviews of this topic; the first in *Pediatric Endocrinology: A Clinical Guide*, edited by F. Lifshitz (1990), and the second in a text entitled *Bailliere's Clinical Endocrinology and Metabolism. Growth Disorders*, edited by J. Bierich (1992). These references are given for readers who may wish to read further concerning the topic.

*The report by Boulton et al is of importance because of the response of depressed children with growth failure to pharmacologic doses of GH (1.2 U/kg/wk), which is significantly more than the physiologic replacement dose (0.3 U/kg/wk) reported by Fraiser and Rallison (*J Pediatr* 1972;80:603) to not increase the growth of patients with PSS. As pointed out by the authors and by Dr. Clarke in his editorial commentary, these children are different from most children reported with PSS in that they secreted normal amounts of GH. The authors, unfortunately, did not comment on the behavioral characteristics of these children, except for depression. The children described by us and others with PSS often had polyphagia, polydipsia, and encopresis; ate and drank from bizarre places such as dog dishes, gorging themselves to the point of vomiting; and were emotionally rejected by their parents. Hopefully, Boulton et al will write a follow-up article or write a letter to the Editor of GROWTH, Genetics & Hormones, providing the psychological and emotional characteristics of the children reported and of their parents. The paper by Boulton et al is an important paper and we need to be able to place it in a better context in relation to other papers published on the topic.*

Robert M. Blizzard, MD