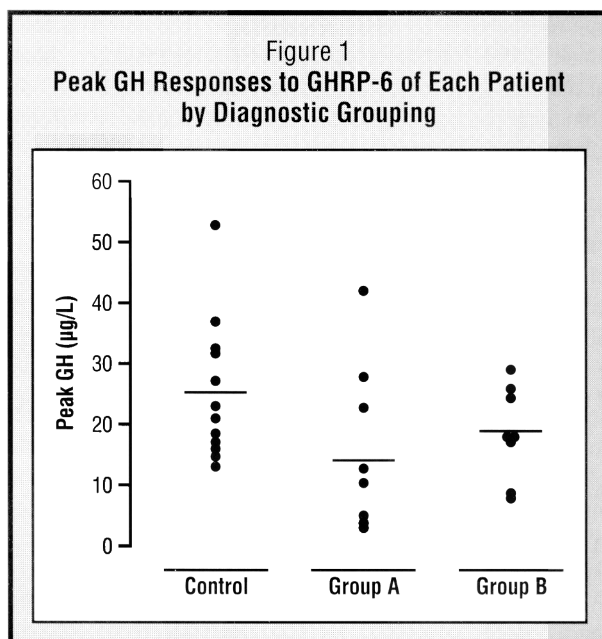
Plasma Growth Hormone Response to Growth Hormone-Releasing Hexapeptide (GHRP-6) in Children With Short Stature

Pombo et al measured growth hormone (GH) levels every 15 minutes (for 90 minutes) following an intravenous bolus of the synthetic hexapeptide GHRP-6 (1 µg/kg). This agent is one of a group of synthetic compounds that have been shown to release GH by a non–GH-releasing hormone (GHRH)-dependent mechanism. The authors tested whether GHRP-6 could be used to diagnose GH deficiency in children with short stature. Three groups of children were studied. The first group (A) included 10 children with idiopathic GH deficiency, as determined by failure of GH levels to rise to 10 µg/L following provocative stimulation. The second group (B) included 8 children with normal GH response to provocative stimuli but with markedly reduced 24-hour integrated GH concentrations. The third group (C) included 12 normal prepubertal children (Figure 1).

All 10 patients in group A showed variable responses to GHRP-6; 50% showed a response > 10 µg/L. In group B, 6 of 8 subjects showed a GHRP-6 response > 10 µg/L. Although there were differences between mean GH secretion in response to GHRP-6 in group A patients compared with normal children, the results suggest that GHRP-6 stimulation is not an adequate method for diagnosing idiopathic GH deficiency.

Pombo M, et al. *Acta Paediatr* 1995;84:904-908.

Figure 1
Peak GH Responses to GHRP-6 of Each Patient by Diagnostic Grouping



***Editor's comment**: Interpretation of these data is that approximately 50% of children diagnosed as having idiopathic GH deficiency by provocative stimuli are able to release GH in response to GHRP-6. Furthermore, 75% of the children with neurosecretory GH deficiency release GH in response to GHRP-6. The authors concluded that GHRP-6 is of no value in diagnosing idiopathic GH deficiency. Perhaps a more provocative conclusion is that the data demonstrate that many children diagnosed with idiopathic GH deficiency have defects in GH secretion rather than GH synthesis. The mechanism of action of GHRP-6 remains controversial. Both a direct effect at the pituitary and/or the hypothalamus by way of somatostatin or GHRH have been suggested. Studies with GHRP-6 have the potential to reveal important information concerning the normal mechanism of GH synthesis and secretion.*

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Does Linear Growth Occur Continuously or as "Saltatory" Growth?

Lampl et al[1] reported that in daily, semiweekly, or weekly measurements of crown-heel length in 31 normal infants followed for 4 to 15 months, linear growth proceeded in a start-stop manner; that is, the infant grew at rapid rates for a brief period of several days, followed by prolonged intervals (average 12 days, but as long as 63 days) without any increase in length. Thus, growth in infancy was not continuous but composed of intervals of stasis and rapid growth, a pattern termed saltatory growth. Heinrichs et al[2] challenged this observation. They measured crown-heel (Harpenden-Holtain infantometer), knee-heel (from photographs), head circumference, and weight of 5 infants (1.6 to 4.2 months) at the same hour of every day for 1 month. These investigators concluded that their data indicated the infants grew continuously in all aspects. By their analyses of direct inspection of individual growth curves, frequency distribution of growth velocities, cumulative probability plots, and correlation of crown-heel and knee-heel growth rates, they could find no evidence for saltatory growth and concluded that growth in infancy was continuous. Lampl et al[3] rebut the observations of Heinrichs et al. They point out the inter- and intra-individual variation in growth pattern in infants in their own data and that 1 month of measurements may have been insufficient to observe saltatory growth in the infants reported by Heinrichs et al. Furthermore, Lampl and colleagues reanalyzed the Heinrichs data and concluded that these infants did indeed display a saltatory growth pattern. For these and other reasons, Lampl et al reject the criticisms of Heinrichs et al.

1. Lampl M, et al. *Science* 1992;258:801-803.
2. Heinrichs C, et al. *Science* 1995;268:442-445.
3. Lampl M, et al. *Science* 1995;268:445-447.