

The Short Child With Subnormal Plasma Somatomedin-C (Sm-C)

The somatomedin-C (Sm-C), or insulin-like growth factor I (IGF-I), level is being used as a screening test for growth hormone deficiency (GHD). To evaluate its diagnostic value, the authors designed a protocol to evaluate: (1) the statistical tolerance limits for Sm-C in children of normal height

between 7 and 10 years of age; (2) the prevalence of subnormal Sm-C in children of the same age who are below the third percentile in height; (3) the prevalence of GHD in children with low Sm-C levels; and (4) the comparison of linear growth responses to hGH treatment between GHD children and hyposomatotropic, non-GHD short children.

Single Sm-C determinations were reported to be of limited value in diagnosing GHD. Only with an average of four determinations (taken at six-week intervals) in seven GHD children could all seven be said to have an average Sm-C level below the 95% lower limit of the tolerance intervals, as based on the mean of one, two, three, or four determinations.

In 97 short non-GHD patients whose Sm-C levels were measured

four times and then averaged, 45% (or 44 children) were below the 2.5 percentile established for normal children. Of these 44 children, who were considered to be hyposomatomedinemic, 12 were classified as GHD, seven as partially GHD, 20 as non-GHD, and five as intermediate in their responses or non-classifiable, as determined by the usual pharmacologic testing. Therefore, 19 of the 44 (or 43% of the hyposomatomedinemic children) and 19 (or 20%) of the 97 children with heights below the third percentile had some degree of diagnosable GHD. The anthropometric measurements and skeletal ages in relation to the chronological ages were identical in the 19 GHD and 20 non-GHD patients, as were the levels of Sm-C. Consequently, the authors deduce that approximately 20% of short children referred to them will be GHD.

Therapy with hGH was given to the GHD and non-GHD hyposomatomedinemic children for six-month alternating periods. During each period, one of four logarithmic dosages were administered: 0.16, 0.26, 0.43, or 0.70 U/kg/wk were given in equally divided doses Monday, Wednesday, and Friday at

10 PM. The results are shown in the table.

The authors report that the two intermediate doses produced significantly different growth rates in the two treatment groups. However, the largest dose produced comparable growth rates in both groups.

The authors speculate that there are several possible explanations for the low Sm-C determinations in the short non-GHD children, including: (1) a relationship to the delayed skeletal maturation, since Sm-C levels increase with age; (2) failure of nocturnal secretion of hGH; (3) impaired production of Sm-C; (4) a bioinactive GH; and (5) an altered Sm-C binding system.

The authors also speculate that non-GHD children will respond to GH therapy in many instances. At conventional GH doses (up to 0.43 U/kg/wk), the magnitude of the response seen in such children was less than 60% as great as that of their GHD counterparts; however, at the dose of 0.70 U/kg/wk, the responses of the four GHD children and the three non-GHD children were comparable.

Rudman D, Kutner MH, Chawla RK: *Pediatr Res* 1985;19:975.

Dose hGH (U/kg/wk)	Increase in growth velocity	
	GHD	Non-GHD
0.16	4.4 ± 0.7 (n = 8)	0.2 (n = 1)
0.26	7.4 ± 1.2 (n = 9)	3.2 ± 0.7 (n = 16)
0.43	8.7 ± 0.9 (n = 12)	5.4 ± 0.7 (n = 12)
0.70	8.3 ± 1.1 (n = 4)	7.3 ± 2.0 (n = 3)

Editor's comment—Although the authors state that four Sm-C determinations were necessary to unequivocally diagnose GHD in the seven GHD patients studied for this purpose, a review of the data of the 28 determinations made in these patients reveals that only two determinations were greater than 0.30 U/ml. Therefore, 26 of the 28 determinations yielded values that were certainly compatible with GHD, although not diagnostic thereof. In

addition, the finding of a low Sm-C (<0.30 U/ml) by averaging four determinations in a short child would be associated with the diagnosis of GHD in only 40% of cases (19 of 44 children in this series). Therefore, the practicing physician can still effectively utilize a single Sm-C determination in evaluating the possibility of GHD. It should be noted, however, that the Sm-C determination is only one facet of the diagnostic evaluation of a short child.