of the mIGF-I in the GHD-1 children reaching peak concentrations on day 5, while in the GHD-2 children there was a brisk increase of the mIGF-I up to day 3, with a decrease on day 4.

**GH treatment**

The GHD-1 and GHD-2 children, both prepubertal and pubertal, had subnormal growth velocities prior to hGH therapy. During treatment with hGH growth velocities increased significantly in both groups (Table 4). Also, the height SDS in the prepubertal and pubertal GHD-1 and GHD-2 subjects improved significantly during treatment with hGH (Table 4).

**DISCUSSION**

In the present study, all the prepubertal and pubertal GHD children (GHD-1 and GHD-2) had a greater increase in IGF-I values during the 5-day IGF-I generation test as compared to the normal-statured and short-statured control children. Although the baseline IGF-I concentrations in the GHD children were significantly lower, they reached similar peak IGF-I concentrations with those observed in the control children. It should be emphasized that this enhanced IGF-I response during the IGF-I generation test occurred in both GHD groups, whether the children had classic GH deficiency (GHD-1) or GH neurosecretory dysfunction (GHD-2). It might be speculated that the enhanced IGF-I response during the IGF-I generation test in the GHD groups was due to a “priming” effect of hGH on an increased amount of available “un-occupied” GH receptors present in GH deficient children.

It is also noteworthy that even though the short-statured control children in our study had similar heights to the GH deficient children, they differed from them in that they had normal growth velocities and normal basal and peak IGF-I concentrations during the IGF-I gen, similar to those of normal-statured children. It should be emphasized that our short-statured control group differed from most Idiopathic Short-estatured (ISS) children included in other IGF-I generation studies in that they had normal growth velocities, whereas the ISS children in the majority of published studies had abnormal growth velocities.

It is of interest to note that the peak IGF-I concentrations occurred more often on days 4-5 of the test in the normal control children, whereas it occurred more often on days 3 and 4 in the GH deficient children. Therefore, it seems important to measure the IGF-I concentrations on each of the five days of the IGF-I gen in order to obtain the peak response of IGF-I in all children. We have previously reported similar findings by applying the IGF-I gen in children with β-thalassemia major. Our findings are in disagreement, however, with a recent study which reported that the peak IGF-I response occurs by 36 hours following a standard dose of hGH.

In ISS, variable results have been reported with regard to the IGF-I response during the IGF-I gen, possibly reflecting the heterogeneity in the etiology of ISS. There are older reports indicating that there is an enhanced response of IGF-I during the generation test in children with ISS. In contrast, another study showed that in 16 ISS patients with normal baseline IGF-I levels there was a lower than normal IGF-I response on days 5 and 8 of a 7-day IGF-I gen, pos-