

± standard error of the mean (SEM) and nonparametric tests were used to determine statistical significance.

Age, weight, height, height velocity, and body mass index did not differ between ISS controls, children with preterminal CRF, and those with ESRD. Bone age was delayed to a comparable degree in all 3 groups. The mean endogenous GH half-life in patients with ESRD was significantly higher than in ISS controls, while that in preterminal CRF patients was shorter than the value in ESRD patients but significantly higher than in ISS controls. A significant inverse linear correlation was observed between GFR and GH half-life. The mean number of detectable GH secretory bursts in ESRD children was greater than in ISS controls and in patients with preterminal CRF, while the interburst interval, the half-duration of the GH secretory burst, and the mean burst amplitude were not significantly different among groups. GH production rate (product of the mean mass of GH secreted per burst and the number of bursts/10 h) was significantly greater in ESRD patients than in CRF patients and tended to be higher than in ISS controls. Both mean and integrated plasma GH concentrations were significantly elevated in the ESRD group compared with the other 2 groups. However, plasma insulin-like growth factor 1 (IGF-1) levels did not vary among groups.

The authors state that the mechanism for increased GH secretion in uremia is unknown, but that the increased frequency of GH bursts is consistent with reduced somatostatinergic inhibitory tone. They theorize that such a decrease in tone could be due to either reduced hypothalamic or pituitary feedback action of IGF-1 or GH itself. IGF bioactivity is known to be reduced in uremic plasma due to the accumulation of binding proteins that are normally removed by renal filtration. This reduced

bioactivity presumably leads to reduced feedback potency of IGF-1. Thus, the increased number of GH bursts, despite the increased GH concentrations, suggests tissue resistance to the actions of GH at the level of the hypothalamus. The authors speculate that the increased number of GH secretory bursts results from attenuated bioactive IGF-1 or GH feedback of the somatotrophic axis and that this suggests an insensitivity to the action of GH in uremia.

Tönshoff B, et al. *Pediatr Res* 1995;37:86-93.

Editor's comment: *This is a very sophisticated analysis of the abnormalities in the GH/IGF-1 axis in children with CRF and ESRD. The authors point out that deconvolution analysis of spontaneous nocturnal GH secretion is exceedingly important to understanding the mechanism of GH secretion and its physiology and pathophysiology in a variety of disorders as well as in normal individuals.*

This particular study answers previous questions concerning the observation of normal IGF-1 and elevated GH levels in children with CRF and ESRD. It also aids in understanding the feedback mechanisms regarding GH and IGF-1 at the level of the hypothalamus and pituitary. However, what remains uncertain is why exogenous GH is so useful in stimulating linear growth in children with CRF. It would be interesting to perform studies similar to those reported in this paper on children before and after exogenous GH administration. Such studies might delineate how exogenous GH affects the GH/IGF-1 axis and its effect on tissue sensitivity to the actions of GH at the level of the hypothalamus.

William L. Clarke, MD

The Detection of Subtelomeric Chromosomal Rearrangements in Idiopathic Mental Retardation

About 3% of the population has an IQ <70; a cause is known in less than half. Chromosomal abnormalities identified by routine cytogenetic analyses account for an estimated 40% of severe mental retardation (MR) and an estimated 10% to 20% of mild MR. Subtle chromosomal defects that are not evident by routine testing could be responsible for a substantial portion of patients in whom a cause for idiopathic MR is not evident. Recent advances in molecular genetic techniques that allow detection of extremely small portions of chromosomes based on analysis of DNA polymorphisms (variable number of tandem repeats, or VNTRs) make it possible to detect such "cryptic" chromosomal defects.

Flint and colleagues used this approach to study 99 patients with idiopathic MR. Their attention focused on the subtelomeric portions of chromosomes because several known MR syndromes have been mapped to these regions and also because lesions in these regions might be repaired by telomeric repetitive DNA, masking the abnormalities from routine cytogenetic detection.

Using highly informative DNA markers that mapped to 28 chromosome tips (normal male karyotype has 48 short and long arm chromosome tips), they found cryptic rearrangements in 3 patients. One had a de novo deletion on the long arm of chromosome 13 and 2 others had de novo deletions of different sizes on the long arm of chromosome 22.

Thus, they found cryptic deletions in about 3% of the patients with MR whom they studied. The authors pointed out that 20 subtelomeric regions were not analyzed. If this was taken into account, together with the facts that the probes were not completely informative and in some instances mapped to regions not as close to the telomeres as they had wished, they estimated that the true frequency of cryptic subtelomeric deletions in MR is at least 6% and probably higher.

Flint J, et al. *Nat Genet* 1995;9:132-139.

Editor's comment: *What do mental and growth deficiency have in common? A lot more than sharing the term "deficiency." Both are multifactorial in their causation. The cause is not known in a high percentage of cases in both instances. They are associated with each other in many instances. Easily detectable chromosomal abnormalities are known to cause short stature and mental retardation, as in Down syndrome. Thus, it is not at all unreasonable to speculate that a substantial portion of "idiopathic" short stature might be caused by cryptic subtelomeric rearrangements as with MR. One has to assume that someone is already looking into this matter, and we look forward to the results.*

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