

this short paper is an important addition to our understanding of the benign course of this disease, the statistics regarding incidence must be regarded as applying only to Olmsted County, Minnesota.

William L. Clarke, MD

Growth in Hemophilic Boys After HIV Infection

Pasi et al measured height and weight 3 times yearly in 26 boys with hemophilia A who became HIV positive during the period from 1981 to 1986. Ten of the boys presently have AIDS-related complex. Height and weight recordings were analyzed over a mean period of 9.2 years, with a mean duration of HIV seroconversion of 4.5 years. Mean growth (height and weight) before and after seroconversion were analyzed in this group by the Wilcoxon matched pairs signed rank test. No significant change in growth or weight was observed after HIV seroconversion. One boy who developed clinical AIDS continued to grow along his respective percentile, and 1 boy with constitutional short stature continued to grow along his respective percentile. Only 1 boy failed to grow along the original percentile, but his growth retardation began 3 years before HIV seroconversion.

Pasi KJ, Collins MA, Ewer AK, et al. *Arch Dis Child* 1990;65:115-118.

Editor's Comment—*This short descriptive paper is the first to document growth in children with asymptomatic chronic HIV infection. As noted by the author, growth failure has been described previously in children with chronic symptomatic HIV infection. The preservation of linear growth in the present sample (up to 6 years) demonstrates the heterogeneity of the complications seen in this syndrome.*

William L. Clarke, MD

Increase in Serum Concentration of Keratan Sulfate After Treatment of Growth Hormone Deficiency With Growth Hormone

Pachman et al measured the serum concentrations of keratan sulfate (KS) in 2 groups of children with short stature: 1 group with constitutional delay and the other with growth hormone deficiency (GHD). The study populations consisted of 14 children between 8 and 11 years of age with constitutional delay and 9 children, ages 8 to 15, with GHD, defined as a peak GH ≤ 10 ng/mL with insulin-induced hypoglycemia, oral L-dopa, or glucagon. The GHD children were growing at a rate < 4 cm/yr whereas the children with constitutional delay were growing > 5 cm/yr, which was nevertheless below the fifth percentile.

In children with constitutional delay, KS averaged 414 ± 118 ng/mL, compared with 505 ± 126 ng/mL in children from a control population (which consisted of 33 children 8 to 11 years old with normal growth). In the GHD children, KS levels were determined at the time of initial evaluation and after 3 to 15 months of GH therapy. These levels initially ranged from 239 to 587 ng/mL, encompassing the levels in the children with constitutional delay. However, 7 of the 9 children with GHD had a rise in KS ranging from 64 to 192 ng/mL during GH therapy. This increase in KS was correlated with an increase in growth velocity.

The authors point out that KS is a glycosaminoglycan that is almost exclusively derived from the metabolism of cartilage proteoglycans and that the amount of KS in the blood is directly proportional to the rate of degradation of cartilage proteoglycans. They previously reported that serum levels of KS rise from a low level in infancy to reach a plateau by age 4 to 5 years. The measurement of serum KS is felt to be an indicator of the response of chondrocytes to IGF-I. The relationship demonstrated between increased growth and increased serum KS suggests that KS may be a reasonable indicator of cartilage proteoglycan metabolism during growth. The authors note that

2 patients with GHD who did not increase their KS levels after GH therapy, despite increases in growth velocity, had pretreatment KS levels at the upper range of normal for age.

Pachman LM, Green OC, Lenz ME, et al. *J Pediatrics* 1990;116:400-403.

Editor's Comment—*Measurement of keratan sulfate (KS) may be a useful indicator of the activity of GH/IGF-I in bone metabolism. These data are somewhat confusing, however, as the increase in KS was relatively modest despite marked increases in growth velocity in the GHD children on GH therapy. This may be due to the heterogeneity of the pretreatment KS levels in this group of children and also to the fact that KS levels plateau in early childhood. The authors correctly point out that an increase in KS indicates a change in the metabolism of proteoglycans, but it cannot be used to predict changes in growth velocity with GH therapy. It is important to remember that IGF-I levels also do not always correlate with response to GH therapy. Nevertheless, it is both interesting and useful to evaluate metabolic changes in bone as a consequence of GH therapy in our attempts to gain a better understanding of how children grow.*

William L. Clarke, MD

Characterization of Dimeric Forms of Human Pituitary Growth Hormone by Bioassay, Radioreceptor Assay, and Radioimmunoassay

Seven highly purified dimeric forms of human pituitary (extracted) growth hormone (hGH) were characterized

from the monomeric forms of 20-, 22-, and 24-kilodalton (kDa) hGH linked together by covalent or non-covalent bonds. Each was studied using 3 different assays: (1) a solid-phase radioimmunoassay (RIA) with rabbit anti-hGH antiserum, the results being expressed in mIU/L by reference to the WHO First IRP 66/217; (2) a radioreceptor assay (RRA) on solubilized bovine liver receptors; and (3) a bioassay (BA) measuring the growth effect on culture of Nb2 lymphoma cells.

These assays produced strikingly different results. In the RIA, all dose/response curves were parallel, except those of the 20-kDa monomeric and the 20/20-kDa dimeric forms. In the RRA, considerable differences appeared in the ability to displace labeled monomeric recombinant hGH from its ligand, with maximal effectiveness for 2 isomers derived from the 22-kDa hGH. The mitogenic effect in the BA was maximal with a non-acidic 20/22-kDa dimer, and minimal with the 20/20-kDa dimer, all the regression lines (number of cells versus log of hormone concentration) being parallel.

Brostedt P, Luthman M, Wide L, et al. *Acta Endocrinol* 1990;122:241-248.

Editor's Comment—*The general sense of the study is that the various molecular forms of GH found in the pituitary—both monomeric (little) and dimeric (big)—have different mobilities in the 3 types of assays used. It is likely that similar observations would be made for the circulating forms of GH. The authors also note that some variants of hGH occur in the pituitary, mainly in dimeric forms. We may conclude from this that measuring hGH is difficult; that the various types of assays may give discrepant results, depending on the molecular forms of the hormone; and that bioassay with Nb2 cells may be relevant for clinical studies.*

Jean-Claude Job, MD

Insulin-like Growth Factors I and II in Healthy Man: Estimations of Half-Lives and Production Rates

The authors measured the half-life of insulin-like growth factors (IGFs) in 2 normal young adult males after a bolus injection of radio-iodinated IGF-I and IGF-II, with measurement of the serum levels of both the free IGFs and the IGFs bound to their specific carrier proteins. They found a half-life of 10 to 12 minutes for free-labelled IGF-I and -II, 20 to 30 minutes for the 50-kDa bound complex, and 12 to 15 hours for the 200-kDa complex.

In a second step of the study, they infused recombinant IGF-I, 20 $\mu\text{g}/\text{kg}$ per hour intravenously, during 6 days in the same subjects and measured the different circulating forms of IGFs by RIA after chromatographic separation. By this means, the calculated production rates were found to be 10 mg/d for IGF-I and 13 mg/d for IGF-II.

This agrees with the earlier findings, by the same group and by others, that the 200-kDa complex contains the major pool of IGF in human serum, and confirms that this

complex is mainly responsible for the relatively long half-life of IGF in humans. It suggests that, besides the main pool of 200-kDa, the free and the 50-kDa IGF pools, which have a rapid turnover and could account for daily IGF production, are the source of a shift toward the 200-kDa pool.

Guler HP, Zapf J, Schmid C, et al. *Acta Endocrinol* 1989;121:753-758.

Editor's Comment—*These physiological data in adult humans are possibly of great importance for the interpretation of measurements of IGFs, mainly of IGF-I, in growing children and adolescents. Probably measurement of free IGF-I and of the 2 main IGF-I carrier protein complexes could reduce the difficulty in correlating the results of routine IGF-I assays with such clinical data as height or growth rate.*

Jean-Claude Job, MD

Comparison of Education and Occupation of Adults With Achondroplasia With Same-Sex Sibs

A common concern to parents of children with achondroplasia is that the children will suffer occupational discrimination when they grow up. To investigate the issue, Roizen and colleagues compared education and occupation levels in adults with achondroplasia to those of same-sex sibs. Information was gathered by interview or questionnaire from 8 affected men and 32 unaffected brothers and from 12 affected women and 35 unaffected sisters. An occupational score was calculated from a subscale of the Hollingshead Four Factor Index of Social Status. No significant differences in age or education were noted between the patients and their same-sex sib. The occupation score for affected men was not statistically different from that of their brothers;

however, the score for affected women was significantly lower than that of their unaffected sisters. Education level was the single most important variable affecting occupation level for both sexes. The authors speculate that physical deformity accompanying achondroplasia (eg, large head size) may be more detrimental in the workplace to women than to men. They stress the need for more research in this area and the need for parents and educators to invest heavily in educating achondroplastic children.

Roizen N, Ekwo E, Gosselink C. *Am J Med Genet* 1990;35:257-260.

Editor's Comment—*As pointed out by the authors, this is a small study, and the data are not sufficient to*