

Report of the Conference on Uses and Possible Uses of Biosynthetic hGH

In a society that values tallness, enormous pressure will be put on physicians to prescribe human growth hormone (hGH). The pressure will come from parents whose children are not fulfilling parental expectations in sports, social interactions, and academic achievement. Physicians will determine whether to prescribe hGH to children who are short because of normal genetic variation. They will be forced to decide whether to tamper with normal children in the hope of making them "better." Is it ethical to administer hGH to short children who are probably not growth hormone (GH) deficient according to current criteria? Will such treatment produce taller or better adults? What are the possible adverse side effects? How will misuse be prevented?

These considerations were addressed by 50 experts at a conference in late 1983 on the uses and possible uses of DNA-hGH. The conferees were asked to address the full spectrum of concerns about uses and abuses of hGH. Underwood summarized the conference findings in an editorial for the *New England Journal of Medicine*.

At the conference, one group addressed the question of how to distinguish partial GH deficiency. Provocative tests are not always reliable in determining whether insufficient GH is the cause of limited growth, since some patients with partial GH deficiency release significant amounts of GH when tested with pharmacologic agents. Participants discussed the increasing interest in measuring serum GH levels under physiologic conditions. Data are insufficient at present to permit judgment of optimal times, duration, and methods of measurement. The participants agreed that somatomedin-C concentrations are sometimes helpful in diagnosis if used in conjunction with other tests. Low values must be confirmed by GH testing before the diagnosis of GH deficiency is made, and low values in young children must be interpreted cautiously.

The terms used to describe short stature were also discussed: normal variant short stature, GH-dependent growth failure, and the syndrome of immunoreactive-bioinactive GH are poor terms.

The potential complications of

glucose intolerance, hyperlipidemia, and possible acceleration of the atherosclerotic process with GH administration were considered. The conferees recommended that an epidemiologic survey of possible late-appearing side effects be undertaken in patients who have been or are being treated with hGH.

The consensus of the conferees was that there is an urgent need for therapeutic trials to determine the effect of GH in short children who do not have GH deficiency. It was deemed ethical to administer GH to such children under a controlled research study. Because no mechanism for direct regulation of prescribing hGH is available, it was agreed that the most effective way to avoid abuses is through the education of physicians and the public.

Underwood L: *N Eng J Med* 1984; 311:606.

Editor's comment—The above abstract is brief, and the interested reader is encouraged to review the entire report. Consideration of this well-reasoned editorial by all physicians who will be prescribing hGH for any cause is imperative.

Comparison of Physiologic and Pharmacologic Assessment of GH Secretion

Siegel et al evaluated and compared growth hormone (GH) release to arginine (ATT), insulin (ITT), and sleep. Samples were drawn every 30 minutes between 11:00 PM or midnight and 6:00 AM via an indwelling catheter. Sixty-two short children (53 males and nine females) were evaluated. Twenty (32%) failed to respond significantly to either test (maximal GH, <3.5 ng/ml). Surprisingly, only 14 of these 20 were classified by the authors as truly and permanently GH deficient. The other six were patients with constitutional growth delay, psychosocial dwarfism, and hypogonadotropic hypogonadism. Five

subsequently had normal peaks during sleep.

Thirty-three (53%) of the 62 responded normally to both the pharmacologic and physiologic tests. Eight (13%) had abnormal responses to pharmacologic testing but normal responses to physiologic testing (mean peak GH = 19.0 ± 2.0 ng/ml). Seven of these eight were growing 5.0 cm/yr or more and were believed to have constitutional growth delay. Only one patient (<2%) failed to respond to physiologic stimuli but responded to pharmacologic stimuli.

These results confirm previous studies that show there is often a discordance in the GH response in normal individuals who are tested with arginine- and insulin-induced hypoglycemia. The authors state that the responses to the two tests were concordant in 43 of 62 patients (69%). However, if the 28 patients

who responded to neither ATT nor ITT are removed, the authors found that only 23 of 42 patients (55%) who responded did so to both stimuli.

These studies verified previous reports that more than one pharmacologic test must be used to diagnose GH deficiency and that physiologic testing (nocturnal frequent sampling) is preferable to pharmacologic testing. The data also reaffirm the impressions of many that even with both tests, erroneous diagnoses are still frequently possible.

Siegel SF, Becker DJ, Lee PA, et al: *AJDC* 1984;138:540.

Editor's comment—These data further emphasize how difficult it may be to diagnose all patients with GH deficiency, and therefore how difficult it is to determine precisely the incidence of GH deficiency.