

Letter from the Editor

This is the 20th issue of *Growth, Genetics, and Hormones*, completing five years of publication. The goals of the Editorial Board have been to assimilate the interests of geneticists, endocrinologists, nutritionists, and pediatricians in respect to the factors that affect growth in children, and to publish articles and abstracts in accordance with these interests. The Editorial Board has received much satisfaction in pursuing its endeavors and expresses its appreciation to Genentech Corporation for the educational grant that has made this publication possible. The Board hopes to continue its efforts in the future; please advise us how we can better accomplish our goals.

For the Editorial Board,
Robert M. Blizzard, M.D.

Special Report: 7th International Symposium on Growth and Growth Disorders

April 21-22, 1989, Rome, Italy

Robert M. Blizzard, M.D.
Chairman
Growth, Genetics, and Hormones

One entire session of this symposium dealt with adult patients with growth hormone deficiency (GHD). Prof. Bjork of Sweden queried 65 adult patients with GHD who were treated with growth hormone (GH) in the past. Twenty-three responded to the questionnaire. There were 47 controls. The conclusion of this inquiry was that patients with GHD were "worse off" than controls with respect to their quality of life. These patients reported that they felt isolated socially, were less active and mobile, had sleep disturbances, and felt less adequate emotionally than the controls. The data suggested that a significant proportion of patients with GHD have psychological damage from their chronic disease. Several individuals from the audience suggested that the control group should not have consisted of normal individuals, but individuals with other types of chronic illness or patients with short stature who were not growth hormone deficient. The various discussants agreed that the GHD patients were handicapped, but there was no way to know how they compared to individuals with other handicaps.

Drs. O.M. Rutherford and M. Preece of London reported

changes in skeletal muscle after discontinuing GH in GHD patients. The study was established because a significant decrease in the cross section of the thigh, as determined by CT scan, was noticed in one patient with GHD who had stopped GH treatment upon becoming an adult. In this study 7 of 8 patients who stopped GH because they were late adolescents or adults experienced decreases in muscle strength and size of the quadriceps. Biopsy demonstrated that the fiber area of the quadriceps was decreased. Interestingly, only one of the subjects was found to have a decrease in triiceps area, and no change in strength was found in this muscle.

Drs. H. Whitehead and D. Hadden of Belfast looked at muscle fiber size in 13 GHD patients 19 to 52 years of age. Seven had been treated with GH, but not for at least 6 months before the study was undertaken. In these patients, GH was adequately replaced with hydrocortisone, thyroxine, and sex steroids. The study was of a double-blind crossover design, in which subjects received GH, 0.5 U/kg/wk divided into daily injections, for 6 months. Eleven of the 13 completed the study. The data from biopsies indicated that 6 months of treatment had no effect on the size or the type of muscle fibers. The authors emphasized that this

was a small population.

Prof. Sonksen of London then discussed the effects of 6 months of GH treatment on body composition in adults with GHD. Twelve subjects received placebo and 12 received GH. Their average age was 30 ± 3 years. Studies included body composition (assessing total body potassium), a CT scan of the thigh, and measurement of various chemical parameters. The results indicated that the lean body mass increased, but fat mass decreased significantly. The fat area in the thigh did not change, but the skin fold thickness decreased by 25%; this decrease was most marked in the abdominal area.

Dr. G. McGauley of London assessed the quality of life before and after GH treatment in adults with GHD. Seventeen GHD patients who received GH were compared to 17 who did not. The former perceived that they incurred less illness and had a better quality of life. The actual measurements of differences were minimal, however.

Prof. J.M. Connor of Glasgow presented an excellent discussion of the molecular genetics of Turner's syndrome. "We must consider DNA analysis as well as chromosome analysis in patients with Turner's syndrome," he stated. Connor reported an interesting observation that in all 14 cases tested, the X chromosome came from the mother. Connor

emphasized that DNA analysis can pick up translocations and that Y material can occur in individuals with XO/XX syndrome. In such individuals gonadectomy is indicated. Y determinants should be looked for in all XO/XX Turner's patients, and this can best be done by DNA probes. Connor stated that 10% of XO/XX girls have unexpected chromosome material. He also noted that 2% of all pregnancies start with 45 XO chromosome karyotype and that the majority of these abort spontaneously.

Prof. R. Rappaport of Paris discussed the theories of growth retardation in patients with Turner's syndrome. The endocrine hypothesis—ie, GHD—was considered first. He carefully reviewed the data from the literature, which he agreed is confusing. He emphasized that complete GHD is rare and explained that the differences in data from various clinics may be related to the fact that GH production is not the same at various stages of preadolescent life, and various investigators have reported on patients of varying ages. Values of integrated GH concentrations in patients with Turner's syndrome must be compared with those of normal preadolescents, as GH production increases in puberty. Rappaport believes that GHD is *not* significant in patients with Turner's syndrome. Furthermore, patients with Turner's syndrome do not respond as well to GH therapy as do GHD patients, and this mitigates against the possible diagnosis of GHD. He then considered the possibility of a chromosomal defect and stated that the genes on the short arm of X and Y are believed to be genes accounting for stature. Absence of these genes will produce short stature. Rappaport also talked about the likelihood of these patients having a primary skeletal defect. He presented histological data collected several years ago by Dr. Scinescu regarding the growth plate cartilage of patients with Turner's

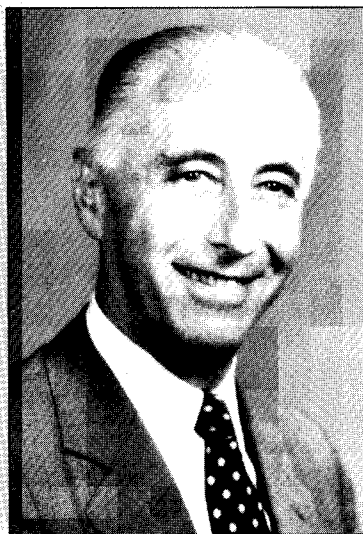
syndrome. Clusters of chondrocytes were found in such patients, and there was abnormal organization of cartilage. In the discussion session that followed, Prof. Bierich of West Germany reported testing 36 patients with Turner's syndrome for integrated concentrations of GH. Several had decreased GH production compared to normals.

Prof. A. Ferrandez of Spain and Dr. R. Rosenfeld of Stanford (USA) then discussed studies of GH therapy in patients with Turner's syndrome. Ferrandez reported that patients receiving GH, GH plus anavar, or GH plus estrogen in small doses had an increase in the cortical thickness of bone and no change in bone age. There also were increases in bone density and in growth. Skin folds decreased in all

groups. Dr. Rosenfeld reported on 4 years of collaborative experience with the Genentech DNA recombinant growth hormone. The summation was that patients with Turner's syndrome receiving GH plus anavar, or even GH alone, are now exceeding the heights projected at the time they began GH therapy.

This conference focused on adult patients with GHD and on patients with Turner's syndrome. Our understanding of Turner's syndrome is now at the point where such patients possibly should have the opportunity to receive GH as a therapeutic agent. However, we will need more information concerning GH production in normal adults before we can conclude that GH is also good therapy for adults with GHD.

Meet the Editorial Board



Associate Editor
Jean-Claude Job, M.D.

Dr. Job is Professor and Chairman of Pediatrics at the Hôpital Saint-Vincent de Paul in Paris. He also heads the pediatric clinic, in which he organized a division of endocrinology.

A leading investigator of biosynthetic human growth hor-

mones in France, Dr. Job developed a research laboratory on human growth under the auspices of the French national institute of health, INSERM, and has served as research director since 1978. He organized the French national committee for hGH (France-Hypophyse), which he served first as secretary and, since 1983, as president. He also established a working group on hGH for the European Society of Pediatric Endocrinology.

Dr. Job earned his medical degree from the University of Paris in 1952. He has published more than 450 papers in French and international medical journals and is the editor of a textbook on pediatric endocrinology.

Dr. Job is a member of the European Society for Pediatric Endocrinology, the Société Française de Pédiatrie, and the Société Française d'Endocrinologie. He is also a corresponding member of the Lawson Wilkins Pediatric Society.