

## Special Report:

# International Growth Hormone Symposium—June 15-18, 1987, Tampa, Florida

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Dr. Barry Bercu (Tampa, Florida) was the primary organizer of this excellent conference. Because of a great deal of material, much of it complex, was presented, this summary highlights only the major points that were covered.

Neuroendocrine regulation of growth hormone (GH) secretion received considerable attention. Drs. Gloria Tannenbaum and Joseph Martin demonstrated very convincingly that GH-releasing hormone (GHRH) is secreted in the posterior part of the hypothalamus (tubero-infundibular region) and that growth hormone-releasing factor (GRF) is secreted in the ventromedial and arcuate nuclei. Somatostatin neurons are located primarily in the anterior hypothalamic region.

Galanin is a recently described neuropeptide of 29 amino acids; its action is additive to that of GRF. Galanin is produced in the ventromedial and arcuate nuclei, and the action is blocked by somatostatin. Dr. Eugenio Muller (Milan, Italy) emphasized that epinephrine is necessary for GH to be released by galanin. Dr. Muller also emphasized the importance of the cholinergic system and demonstrated that GH release in response to exercise, arginine, and clonidine is blocked by atropine. Clonidine, an  $\alpha_2$  adrenergic agent, was used by Muller and his co-workers to increase GH production and increase growth velocity over six- and 12-month periods in at least some children with severe short stature.

Dr. Alan Rogol presented data obtained from 20 patients who were treated with GRF in an international collaborative study. Dr. Rogol stated, "A more potent analog is needed if GRF is to be a valuable therapeutic agent." However, GRF remains a very valuable study tool for those interested in neuroendocrine interrelationships.

Dr. John Phillips discussed the presence of the two GH and three HCS genes on chromosome 17. Recently, a placental GH (derived from the hGH-V gene) has been described. This is a 22 K pituitary GH with 13 substitutions. A poster submitted by Frankenne et al demonstrated that GH was not present in amniotic fluid or in fetal serum. This produced some skepticism regarding the possible role of this hormone as a fetal GH. Dr. Phillips indicated that the first CMS gene is inactive and that apparently none of the GH or HCS genes are necessary for survival.

Drs. Gerald Baumann and James Lewis discussed the various forms of monomeric hormone in the pituitary and in serum. The human growth hormone (hGH)-N gene is responsible for production of both 22 K and 20 K GH. The latter has minimal immunologic and growth-promoting activity, but does have diabetogenic activity. Dr. Lewis concluded, "Although the number of GH variants and modifications have reached eight, there are at least an equal number of unidentified forms in pituitary extracts." A most intriguing part of Dr. Baumann's presentation was

his description of two binding proteins for GH found in plasma. The function of these binding proteins remains unknown, but there is some indication that one or both of these proteins could be receptor related and that even a partial portion of the receptor passed into the serum.

Dr. Hiroo Imura described a highly innovative sandwich enzyme immunoassay to measure GH. The assay's lower limit of sensitivity equals 50 pg/ml. Since GH is found in nearly all normal individuals at all times, Dr. Imura utilizes this assay, which he developed with his co-workers, in diagnosing GH deficiency and acromegaly. Using this technique to measure GH in urine enhances its diagnostic capability. Dr. Imura also determined that the kidney plays an important role in the degradation of GH.

Several experts discussed human insulin-like growth factor (IGF)-I and IGF-II. Dr. Matthew Rechler and others are exploring the possibility, which seems more likely to be a probability, that IGF-II plays a role in fetal growth. Drs. John Sussenback and Michael Czech discussed the role of the IGF-II gene and receptors, respectively, in the fetus and the neonate. Their data tend to substantiate an important role for IGF-II in fetal growth.

Drs. Olle Isaksson, Rudolf Froesch, and Naomi Hizuka individually presented data comparing the effects of GH and IGF-I on skeletal growth. IGF-I, as dem-

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onstrated by Hizuka and Froesch, has a growth-promoting effect on the tibial plates of hypophysectomized rats. Isaksson infused GH locally on one of the epiphyseal plates, that of the right femur, and demonstrated unilateral growth in that femur. His thesis is that GH stimulates colony formation of epiphyseal chondrocytes adjacent to the epiphysis, while IGF-I stimulates cells isolated both in the proximal and intermediate parts of the growth plate.

Dr. David Clemmons studied the metabolic action of GH in relation to nutrition and reported that IGF-I levels do not fall in obese individ-

uals with low energy diets; they do fall in individuals who are not obese. Their preliminary data suggest that administration of GH at 0.1 IU/kg body weight every other day does not enhance weight loss in obese individuals.

Dr. Kerstin Albertsson-Wikland presented data suggesting that integrated concentrations of GH are directly proportional to the height of children both in pubertal and prepubertal stages. Dr. Barry Bercu recapitulated his extensive studies of short children with regard to GH concentrations in serum over 24 hours.

GH neurosecretory dysfunction was discussed extensively. Most agreed that this is an appropriate term for patients who have been exposed to cerebral irradiation

and who have dysfunction of GH secretion. However, many investigators are not ready to apply the term to other entities in which there may be diminished GH secretion.

Dr. Raphael Rappaport studied the effect of cranial irradiation on GH secretion and growth in a large number of patients and reported that slowing of growth usually does not occur until at least 18 months after brain irradiation. Patients receiving spinal plus cranial irradiation have greater limitation of growth potential than do those who receive cranial irradiation alone.

Those interested in purchasing a copy of the published proceedings of this conference should contact Dr. James Posillico of Serono Symposia USA at 800-225-5185.