QUANTITATION OF IMMUNOREACTIVE GH (IRGH) IN URINE

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The output of IRGH was measured in timed urine collections obtained from children with normal and abnormal growth. This information was compared to data obtained from determinations of plasma GH during pharmacologic stimulation. 86 children (ages 2-17 years) collected 12 hour overnight urine specimens. Group I included healthy controls. Group II comprised children with height >-2 S.D., growth < 5 cms/year, and peak GH > 8 ng/ml to stimulii. Group III consisted of GH deficient children.

50 ml aliquots of urine were dialyzed and concentrated 50 fold by lyophylization using a modification of the method of Hansen. Recovery of added GH ranged from 80-100%. IRGH was measured by a routine double antibody radioimmunoassay. The quantity of IRGH excreted was standardized for weight (ng/kg).

Results: Urine IRGH ng/kg (mean ± sem)

	Group I	n	Group II	n	Group III	n
All	0.26 ± .02	33	0.17 ± .02	29	0.10 ± .01	24
Prepubertal	0.28 ± .03	18	0.17 ± .03	14	0.08 ± .02	11
Pubertal	0.23 ± .03	15	0.17 ± .03	15	0.12 ± .01	14

Healthy children (Group I) excrete significantly greater amounts of IRGH/kg than children in groups II or III ($p < .01$). Group II had significantly higher IRGH/kg compared to Group III ($p < .03$). Similar quantities were excreted in prepubertal and pubertal subjects.

Urine IRGH in Hypopituitary Patients Pre and Post GH Injection

Baseline	n	0-12 h Post Injection	n	13-24 h Post Injection	n
.14 ± .02	14	.37 ± .06	14	.13 ± .02	7

Conclusion: Pathologically short children who are GH deficient or GH sufficient by standard provocative tests, excrete less urine IRGH than control subjects. Sex steroids do not appear to augment urine IRGH. Urine IRGH measurements may prove useful for monitoring compliance during GH treatment.

423 HIGH INCIDENCE OF PRENATAL AND PERINATAL MEDICAL COMPLICATIONS ASSOCIATED WITH GROWTH HORMONE NEUROSECRETORY DYSFUNCTION (GHND). Barry B. Bercu, Dorothy I. Shulman, Allen W. Root. Department of Pediatrics, University of South Florida College of Medicine, All Children's Hospital, St. Petersburg, FL 33731

An increased incidence of perinatal problems has been reported in classical GH deficiency. We describe a similar association in children with GHND. Mean 24h GH concentrations were 2.0 ± 0.1 ($\bar{x}$ ± SE), 1.6 ± 0.2 and 4.6 ± 0.4 for GHND (n=17), GH def (n=15) and control (n=20) groups. Using cluster analysis, the number of GH peaks was intermediate for GHND (6 ± 1) between classical GH def (5 ± 1) and control (8 ± 0) children. The number of low amplitude GH pulses (peak<5 ng/mL) was highest in GH def and there was a greater number of higher amplitude GH pulses (peak 5-<10, 10-20, >20ng/mL) in GHND compared to classical GH def but less than controls. Of 17 GHND patients, 11 had significant problems: 1) twin conceptus lost at 15 wk. gestation, 2) fetal bradycardia with meconium staining, 3) septo-optic dysplasia with RDS, hypoglycemia, hyperkalemia, 4) SGA after 2 intrauterine blood transfusions, hypoglycemia, respiratory distress, 5) hyperbilirubinemia requiring exchange transfusion, 6) SGA, jaundice following hemorrhage during pregnancy, hypoglycemia, respiratory difficulty, 7) fetal distress, jaundice, 8) "very premature appearing newborn" although full term by dates, 9) abruptio placenta, 10) 1 minute apgar of 4, 11) neonatal jaundice. These data suggest that there are quantitative and qualitative differences in GH pulses between GH def and GHND children. GHND children, as in classical GH def, have GH secretory abnormalities frequently due to prenatal and perinatal complications.

424 DECREASED GROWTH HORMONE (GH) BINDING TO IM-9 CELLS IN CHILDREN WITH BIOLOGICALLY INACTIVE GH SYNDROME (BI). Tzvy Bistritzer, Stuart A. Chalew, Judith C. Lovchik, A. Avinoam Kowarski, University of Maryland School of Medicine, Department of Pediatrics, Baltimore, MD.

We measured the ratio of radioreceptor assayable (RRA) to radioimunoassayable (RIA) GH in: a/ Fifteen normal stature children and young adults (controls). b/ Seven poorly growing children (neurosecretory; NS) who had normal GH RIA responses to stimulation but deficient 24-hour integrated concentration of GH (IC-GH). c/ Six poorly growing children (bioinactive; BI) who had normal GH secretion both to stimulation and IC-GH. The BI group was 9.1±3 (mean ± SD) years of age, bone age 6.1±2.7 years, IC-GH 6±2.4 ng/ml (normal 3.2-12). On GH therapy the growth rate of BI patients increased from 3.2±0.5 cm/yr to 8.8±1.9 cm/year.

RRA was a modification of a previously reported RRA using IM-9 lymphocytes. The RRA/RIA was 1.3±0.4 in controls, 1.5±0.7 in NS and 0.6±0.6 in BI patients. The difference in RRA/RIA between BI patients and controls was significant ($P<0.005$).

We conclude that 1/ The circulating GH of NS patients has a normal binding affinity to IM-9 cells. 2/ Decreased binding to IM-9 cells may be a clinically useful diagnostic test for BI.

● 425 HUMAN GROWTH HORMONE VARIANT (hGH-B) PROMOTES GROWTH IN TRANSGENIC MICE. Sandra L.Blethen[1], Richard F.Selden[2], Fred I.Chasalow[1], Thomas E.Wagner[3], Jeung S.Yun[3], Howard M.Goodman[2]. [1]Sch of Med, SUNY Stony Brook, Schneider Children's Hosp of LIJMC, Dept of Peds, New Hyde Park, NY; [2] Harvard Med Sch, Mass General Hosp, Dept of Mol Biol, Boston; [3] Ohio Univ, Athens, OH.

The human growth hormone (hGH) gene family consists of 5 members linked on the long arm of chromosome 17. The hGH-A gene is expressed by the somatotrophs of the anterior pituitary. The hGH-B gene encodes a GH-like polypeptide of unknown function. To determine if hGH-B is capable of stimulating growth in animals, transgenic mice containing a metallothionine-I/hGH-B fusion gene were generated. The GH produced by these mice was compared with pituitary hGH-A, mouse GH, and hGH-A and hGH-B from transfected mouse L cell fibroblasts. The 3 transgenic male mice were larger at weaning (26-31 gms) than control males (20 ± 0.4 gms); by age 2 mos the transgenic mice were 40-90% larger than the controls. Serum from these mice contained large (17-30 µg/ml) amounts of hGH-immunoreactivity while control serum did not. The GH-immunoreactivity from the transgenic mice differed from hGH-A in a) cross-reactivity with a panel of monoclonal antibodies, b) behavior on gel filtration and c) pI. Conclusions: hGH-B is capable of stimulating growth in mice. The differences in amino acid sequence between hGH-A and hGH-B result in substantial differences in tertiary and quanternary structure.

426 ACROMEGALY PRESENTING IN INFANCY. Denise Blumberg, Charles Sklar, Jennifer Bell and Raphael David. New York University and Columbia Presbyterian Medical Centers, Departments of Pediatrics, New York, New York.

We report a female child with a growth hormone (GH) secreting pituitary adenoma and hyperprolactinemia, diagnosed at 21 months, but with clinical signs in early infancy. Macrocephaly was noted at 3 months, and by 21 months head circumference was 55 cm (+5.5 SD). Linear growth was accelerated by age 6 months, and at 21 months height was 98 cm (+4.4 SD). CT scans at 21 months showed a pituitary tumor with suprasellar extension. Following complete surgical removal, immunohistochemical staining of the tumor tissue was positive for GH but not prolactin (Prl). Pertinent hormonal data demonstrated the following basal serum levels:

	GH (ng/ml)	Prl (ng/ml)	Sm-C (ng/ml)
Preoperatively	135; 82	565; 230	1540 (nl 18-97)
1-2 wks. postop.	1.7-4.7	27	221
1½ yrs. postop.	2.8-4.1	81 - 101	56; 111

Growth velocity has remained normal (6 cm/yr) despite persistently low levels of GH (max 4.3 ng/ml following insulin, L-Dopa and arginine). TRH stimulation failed to elicit a rise in either GH or Prl. We suggest that increased Prl resulted from hypothalamic damage, and we speculate that it is responsible for normal growth and Somatomedin-C (Sm-C). There has been no recurrence to date (age 3½ yrs). To our knowledge, this is the youngest verified case of acromegaly reported.

427 DOSE-RELATED SUPPRESSION OF LH RESPONSE TO LHRH AND CLINICAL PARAMETERS BY NAFARELIN, AN INTRANASAL GnRH ANALOG. R. Brzyski, C. French, F. Comite. (Spon. by M. Genel). Yale University School of Medicine, Departments of Pediatrics and OB/GYN, New Haven, CT.

Twelve children (10 girls, 2 boys)with precocious puberty were treated with Nafarelin, an intranasal GnRH analog, for 6 months. Seven patients (mean age of 6.8 yrs) received 800 mcg and five patients (mean age of 7.8 yrs) received 1600 mcg daily at night. Standard LHRH tests were performed and secondary sex characteristics were assessed at 0, 3, and 6 months of therapy. Results are reported as mean ± SE.

Dose	Peak LH (mIU/ml) 0	3mos	6mos
800 mcg	41.4±7.7	8.0±0.6	7.2±0.4
1600 ug	24.7±7.7	6.1±0.6	6.4±0.4

At 3 months of therapy the higher dose of nafarelin produced a significantly greater ($p<.05$) suppression of peak LH levels during the LHRH test. These differences were not significant by six months of therapy. Regression of breast development and reduction in pubic hair appeared to occur earlier in the children treated with the higher dose. These data suggest that the higher dose of Nafarelin may initiate a more rapid suppression of serum LH response and normalization of pubertal development. Follow-up studies are essential to determine if a more rapid decrease in LH will have a long-term impact on growth dynamics in children with precocious puberty.