- 422** **QUANTITATION OF IMMUNOREACTIVE GH (IRGH) IN URINE**
Christine Albini, Teresa Quattrin and Margaret H. MacGillivray
SUNYAB, Buffalo Children's Hospital, Dept. of Pediatrics, Buffalo
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 SD, growth <5 cms/year, and peak
GH >8 ng/ml to stimuli. Group III consisted of GH deficient children.

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

Results: Urine IRGH ng/kg (mean $\pm$ sem)

	Group I	n	Group II	n	Group III	n
All	0.26 $\pm$.02	33	0.17 $\pm$.02	29	0.10 $\pm$.01	24
Prepubertal	0.28 $\pm$.03	18	0.17 $\pm$.03	14	0.08 $\pm$.02	11
Pubertal	0.23 $\pm$.03	15	0.17 $\pm$.03	15	0.12 $\pm$.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 $\pm$.02	14	.37 $\pm$.06	14	.13 $\pm$.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 COM-
PLICATIONS ASSOCIATED WITH GROWTH HORMONE NEUROSECRET-
ORY DYSFUNCTION (GHND).** Barry B. Berdu, 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
($\bar{x} \pm SE$), 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, >20 ng/mL) in GHND compared to classical GH def but
less than controls. Of 17 GHND patients, 11 had significant prob-
lems: 1) twin conceptus lost at 15 wk. gestation, 2) fetal brady-
cardia with meconium staining, 3) septo-optic dysplasia with RDS,
hypoglycemia, hyperkalemia, 4) SGA after 2 intrauterine blood
transfusions, hypoglycemia, respiratory distress, 5) hyperbili-
rubinemia requiring exchange transfusion, 6) SGA, jaundice follow-
ing hemorrhage during pregnancy, hypoglycemia, respiratory diffi-
culty, 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 Bistrizer, Stuart A. Chalew, Judith C.
Lovichik, A. Avinoam Kowarski, University of Mary-
land School of Medicine, Department of Pediatrics,
Baltimore, MD.

We measured the ratio of radioreceptor assayable (RRA) to
radioimmunoassayable (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 $\pm$ SD) years of age, bone age 6.1 ± 2.7
years, IC-GH 6.2 ± 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,
Richard E. Selden, Fred I. Chaslow, Thomas
E. Wagner, Jeung S. Yun, Howard M. Goodman.
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 metallothionein-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 ($17-30$ μ g/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 quaternary 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 cir-
cumference 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, immunohistochem-
ical staining of the tumor tissue was positive for GH but not
prolactin (Prl). Pertinent hormonal data demonstrated the follow-
ing 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
1 1/2 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 3 1/2 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 $\pm$ SE.

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