P. Rochiccioli, V. Moisan*, M. Tauber*, C. Pienkowski*

Service de Pédiatrie, Unité d'Endocrinologie –
CHU Rangueil – Toulouse – France

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GROWTH HORMONE DEFICIENCY AND NEUROSECRETORY DYS-
FUNCTION IN INTRA-UTERINE GROWTH RETARDATION (IUGR)

Growth hormone (GH) deficiencies are rarely reported in IUGR.
Investigation of GH secretion by pharmacological tests (clonidine
+ betaxolol and glucagon + betaxolol) and study of 24-hour GH
secretion was performed in 20 children with growth retardation
and suspected IUGR, defined as birth size (BS) and birth weight
(BW) below the 10th percentile for gestational age. Average age at
consultation was 5½ yr (2-11 yr) and growth retardation -3.1 SD
(-2 to -4.5 SD). Mean birth size was 43.6 $\pm$ 2 cm. In 16 children
the growth curve showed recovery up to 1 or 2 yr followed by
varying degrees of decrease in growth velocity, and in 4 children
growth was steady.

GH deficiency was absent in 7 cases and present in 13 : 2 total
deficiencies (2 tests $\langle$5 ng/ml and IC $\langle$2 ng/ml), 3 partial defi-
ciencies (2 tests $\langle$10 ng/ml and CI $\langle$3 ng/ml), 2 dissociated
deficiencies (1 test $\langle$10 ng/ml and one $\rangle$10 ng/ml with IC $\langle$3 ng/ml)
and 6 cases of neurosecretory dysfunction (both tests $\rangle$10 ng/ml
and IC$\langle$3 ng/ml). SmC was low at 0.8 $\pm$ 0.2 U/ml but this was not
constant.

These data showed that study of 24-hour GH secretion is thus
of value showing that GH deficiency is frequent in IUGR (13/20)
and is very often due to neurosecretory dysfunction (6/13).
GH therapy is thus a possibility for these children.

C. Volta, L. Ghizzoni*, A. Lamborghini*, P. Azzali*,
S. Bernasconi, G. Giovannelli.

Department of Pediatrics, University of Parma, Italy.

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24 HRS. GROWTH HORMONE INTEGRATED CONCENTRATION (IC-GH) AND
GH RESPONSE TO GH-RELEASING HORMONE (GHRH) IN CONSTITUTIONAL
GROWTH DELAY (CGD),TURNER SYNDROME AND GH DEFICIENCY.

The GH response to GHRH and 24 hrs. integrated concentration have been measured in
25 prepubertal children. 12 of them (group 1) were affected by CGD (short stature,
normal height velocity, delayed bone age and GH response to pharmacological stimu-
li $>$10 ng/ml); 7 girls (group 2) had gonadal dysgenesis (with normal GH response
to pharmacological stimuli) and 6 patients (group 3) were GH deficient. Mean IC-GH
and peak GH serum level in response to GHRH stimulation were significantly diffe-
rent among the 3 groups (IC-GH:6.76 in group 1 vs. 4.7 in group 2 vs. 1.64 ng/ml
in group 3, p $<$ 0.002; peak GH 36.6 vs. 21.9 vs. 4.8 ng/ml, p $<$ 0.002). Moreover
the GH Δ values and the area under the curve after GHRH were significantly lower
in group 2 and 3 compared to group 1 (Δ :10.5 and 4.1 vs. 32 ng/ml; area:511 and
291 vs. 1771 ng/ml/90'). No differences were found between group 2 and 3.
Considering the 25 patients althogether, a positive correlation was present bet-
ween GH peak, Δ and area values after GHRH and IC-GH (r:0.6,0.56 and 0.57 respec-
tively). The results of the present study show that : 1) An impairment in GH secre-
tion is often present in patients with Turner syndrome also before puberty.
2) This alteration is more evident in the GH response to GHRH being its Δ and area
values not different from those of GH deficient children. IC-GH levels even if
lower than in CGD group as a mean, show an overlapping in the single values in
these 2 groups.

L. Even*, P. Hertz*, M. Silbermann*, Z. Hochberg.
Departments of Anatomy and Pharmacology, Family Institute
for Research in the Medical Sciences, Technion-Israel
Institute of Technology, Haifa, Israel.

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SEXUAL DIMORPHISM OF GH SECRETION II: THE EFFECTS OF
GRF, SOMATOSTATIN (SST) AND IGF-I.

We have shown that female(F) rat pituicytes were more sensitive to GRF
but that male(M) cells responded more vigorously, and how these changes
were dependent on sex steroids (ESPE 1987). To further study the effects
of sex steroids 22-day-old rats were gonadectomized, and 12 days later
their pituitaries dispersed and treated in vitro for 6 days with 5nM
estradiol(E-2) or testosterone(T). After adherence to cytodex beads, cells
were superfused in 1ml-4 million cell columns. One min. pulses of 6nM
GRF produced 130% increment of GH secretion. In the F cells the basal
secretion of E-2 treated cells was higher by 105% and the response to
GRF greater by 230%, while T had no effect. In M cells T augmented GH
response to GRF to 560%, while E-2 had no effect. In plated M pituicytes
1nM SST inhibited GH secretion by 75%. This was additive with the effect
of GRF, which by 3nM overcame SST. In E-2 treated cells 64% inhibition
with SST was also overcome by 3nM GRF. .. In pituitary cells which were
treated by T, inhibition was only 34%, and overcome by 0.03 nM GRF.
IGF-I induced a dose dependent inhibition of GH basal secretion with
maximal decrease of 31-35% at 0.5 U/ml. The acute response to GRF was
only mildly blunted by IGF-I (8-24%). In E-2 treated cells inhibition of
GH basal secretion required 5-fold higher IGF-I conc., maximal inhibition
was 15-49%, and acute GH response to GRF was blunted by 18-47%. In T
treated cells IGF-I inhibited basal secretion by 48-57% but GH response
to GRF was augmented by 24-55%. It is concluded that the rat pituitary
acquires its sexual dimorphism of GH secretion perinatally. The unique
pattern of GH secretion of each sex is later induced by sex steroid
effects on the pituicytes' response to GRF, SST and IGF-I.

L. Cavallo, A. Acquafredda, N. Laforgia, R. Russo, L. Piacente.
Institute of Clinical and Preventive Pediatrics. University of
Bari, Italy.

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EVALUATION OF GRF TEST IN GH-DEFICIENT CHILDREN.

We determined GH release after 2 GRF tests (synthetic GRF, 1-44s, Sanofi, France)
with 1 (GRF1) and 2 (GRF2) μg/Kg i.v. in 14 clinically prepubertal children
affected by a partial (GH peak between 3 and 7 ng/ml) (PIGHD) (6 children) or
total (GH peak $<$ 3 ng/ml) (TIGHD) (8 children) isolated idiopatic GH-deficiency.
GRF tests were performed in a casual succession with a 24 hour interval, at 9 a.
m.. 9 children had a GH peak $>$ 10 ng/ml (R): 6 children to both GRF tests and 3
children only to GRF1 (in 1 case it was the 1st test and in 2 cases the 2nd one);
5 children had a GH peak $<$ 10 ng/ml to both GRF tests (no-R). All PIGHD and 3
TIGHD were in R-group. GH peak was higher in PIGHD (18.7 $\pm$ 9.2 ng/ml) than in
TIGHD (9.2 $\pm$ 6.1 ng/ml) (p $<$ 0.05). No significant correlation was found between
GH peaks during conventional tests and GRF tests in R-group. Our data show that:
-1 μg/Kg of GRF i.v. is able to evoke the serum maximal GH increase –there is no
difference in GH peak according to the sequence of GRF stimulation and to the sex
-R and no-R show a similar pattern of growth both before and during GH therapy
-chronological, height and bone age do not affect the GH release after GRF -TIGHD
is more frequently pituitary-dependent than PIGHD. We conclude that GRF test is
not a reproducible test in GH-deficient children; therefore it is necessary to
repeat it at least twice to exclude a hypophyseal source of GH-deficiency.

J.Cl. REITER*, M. CRAEN, G. VAN VLIET
Departments of Pediatrics, Université Libre de
Bruxelles and Rijksuniversiteit Gent, Belgium.

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Growth hormone (GH) response to growth hormone
releasing factor (GRF) in Turner Syndrome.

Growth hormone deficiency has been described in association with
Turner Syndrome, but its mechanisms are unknown.
Seventeen prepubertal girls with Turner Syndrome (age 6 5/12 to
15 8/12 years; height - 5,4 to -1,8 SD; weight 93% to 169% of
ideal body weight - IBW -) underwent a stimulation test with GRF
(0,5 mcg/kg). Plasma GH was measured by radioimmunoassay from
- 30 to + 120 minutes. These responses were compared to those
we previously reported in children with constitutional short
stature - controls - (Hormone Res. 22 : 32, 1985).
Peak Plasma GH after GRF was 17,0 $\pm$ 3,6 ng/ml (mean $\pm$ SEM),
significantly lower (p < 0,001) than in control children
(39,2 $\pm$ 5,1 ng/ml). In Turner patients, peak GH value was
negatively correlated with the % of IBW (r=-0,58, p < 0,02), the
% of body fat (r=-0,59, p < 0,02) and the body mass index
(r=-0,54, p < 0,05). Baseline plasma insulin-like growth factor
(IGF-I) was within the normal range for prepubertal children,
with a mean $\pm$ SEM of 0,77 $\pm$ 0,09 U/ml.
In conclusion, prepubertal girls with Turner Syndrome have a
blunted GH response to GRF; in contrast to children with hypo-
thalamo-pituitary insufficiency, they have normal plasma IGF-I.
Our data suggest that the decreased GH response to GRF of
Turner Syndrome patients may result from excess body fat.

F. Galluzzi*, R. Salti*, S. Seminara*, G. Merello*,
C. Botti*, P. Becherucci*, C. La Cauza* (Introd. by E.
Cacciari)
Department of Pediatrics – University of Florence – Italy

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RESPONSIVENESS OF PITUITARY hGH TO GRF IN JUVENILES
WITH SIMPLE OBESITY.

It has been found that in obesity the response of plasma hGH to
the pharmacological stimuli is blunted and the episodic output
of hGH during sleep is also subnormal. The response of plasma
hGH to an iv bolus of insulin (4 U/m^2) and to an iv bolus of GRF
(1 mcg/Kg) too and the response of TSH to an iv bolus of TRH
(7 mcU/Kg – 200 mcg maximum dose) were studied in 15 males and
females aged 5 – 10 years, all of whom were suffering from se=
vere simple obesity and in 11 normal subjects of the same age.
The results (mean and SE) were, in obese: peak plasma hGH to in=
sulin hypoglycemia: 6.5±1.4 ng/ml and to GRF: 10.1±1.9* ng/ml;
the peak plasma of TSH to TRH was 18.8±2.5 mU/ml. In the con=
trols they were: 14.0±3.8 ng/ml, 18,3±1.2* ng/ml and 21.6±2.2
mcU/ml respectively. Altough not statistically significant with
respect to the controls, hGH response to insulin hypoglycemia
was lower in obese subjects and hGH response to GRF was markedly
impaired (P< 0.001)* These data seem to suggest that the decrea
sed response to insulin hypoglycemia in obesity is mediated by
an impaired pituitary response to growth hormone – releasing
factor.