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EVALUATION OF GROWTH HORMONE (GH) SECRETION IN SHORT
CHILDREN : SLEEP SECRETION AND STIMULATION TESTS.

GH sleep secretion (SS) and GH response to pharmacologic
stimuli (PS) were compared in 215 short children (-3.2 ± 0.9 SD),
aged from 2 to 18 years (147 boys, 68 girls), 123 at pubertal
stage P1 and 92 P2. Somatomedin C (SmC), DHA sulfate (DHAS),
testosterone (T) or estradiol (E2) were measured. SS and PS were
slightly correlated at both stages P1 (r = 0.4 ; p< 0.01) and
P2 (r = 0.31 ; p <0.01), SS being higher at P2 than at P1. SS is
related to growth velocity at P1. At P2, SS is positively
correlated to T in boys and negatively to E2 in girls. SmC is
correlated to SS and PS at P1 and P2, and is higher at P2. It is
not significantly correlated to sex steroids. SS and PS are
discrepant in 67 cases : either normal SS and low PS in 37 or the
contrary in 30, and moreover SmC level did not rise at P2 in
these patients. Some of the patients with such discrepancies
enhanced their growth velocity under hGH treatment. It is
concluded : 1/ Early pubertal increase of SS preceeds that of
PS. It is controlled by sex steroids. 2/ SmC is related to SS
and puberty, but there may be other regulation factors than sex
steroids. 3/ SS/PS discrepancy was observed in 30 % of cases in
this study. 4/ In these cases, SmC does not rise at P2 and hGH
treatment may improve the growth velocity.

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ADVANTAGES OF THE hGH 24hr SECRETORY PATTERN IN
DISTINGUISHING GROWTH DISORDERS.

We performed a comparative study of 24hr hGH secretion vs. sti-
mulation tests in 48 pts. (29M, 19F) with growth disorders, di-
vided into 5 groups: GR 1 – organic CNS disorder, no hGH; GR 2 –
partial GH def., low hGH; GR 3 – short stature, normal hGH; GR 4
idiopathic high hGH; GR 5 – Laron type dwarfism, very high hGH.

GR	n	A g e yrs	*A-IC ng/ml m±SD	Max. Pulse ng/ml m±SD	No. Pulses >5 ng/ml range	hGH Rise Provocat. Tests
1	14	10-21	0.98±0.2	–	–	14 pt. –
2	14	7-20	1.96±0.5	7.8±2.6	1 – 3	3 pt. 11
3	15	5-19	4.50±0.8	24.7±7.2	2 – 6	15 pt.
4	3	10-11	13.60±4.0	67±22	5 – 7	3 pt.
5	2	19,21	33.9; 45.6	164; 280	9, 7	2 pt.

(*A-IC is the average of 48 samples drawn every 30 min. with a
Cormed continuous withdrawal pump.) By all parameters the groups
differ significantly. Differences in pulse amplitude between
groups 1 & 2 are more distinguishable. Various patterns of rhyth-
micity were observed by cosinor and power spectra analysis. The
present study indicates that the analysis of the hGH 24hr secre-
tory pattern is a more sensitive discriminator of the GH-RH-hGH
axis than provocative tests.

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SHORT SUBNORMALLY GROWING CHILDREN WITH NORMAL GH
RESPONSE TO PHARMACOLOGICAL STIMULI: PHYSIOLOGICAL
GH SECRETION AND RESPONSE TO GH TREATMENT.

We have investigated 16 (3F,13M) prepubertal children, mean
age 8.65 years (range, 4.76 - 10.95) who had a mean height SDS of
-2.90 (range, -4.61 to - 1.83). Mean height velocity SDS was -1.19
(range, -2.13 to-0.41). None had evidence of psychosocial
disturbance. Patients were selected because they had normal
responses (peak GH > 20 mU/1) to pharmacological stimuli of either
glucagon, clonidine or insulin induced hypoglycaemia; mean peak GH
attained to pharmacological stimuli was 27.5 mU/1 (range, 20.1 - 40).

All patients had an overnight serum GH profile, with blood
drawn from an indwelling intravenous cannula at 15 minute
intervals between 1800 - 0800 hrs. GH secretory dynamics were
analysed using PULSAR computer programme. All children (except
one) produced adequate spontaneous nocturnal pulsatile GH
secretion. None of the children had fast frequency
"neurosecretory dysfunction". 15 (3F,12M) were treated with
bio-synthetic methionyl human GH in a regimen of 2 units
subcutaneously daily. All have been treated for periods in
excess of 6 months, and have responded by an increased height
velocity SDS, mean +3.31 (range,-0.21 to + 6.27).

This study points to the difficulty of interpreting
pharmacologic and physiologic testing of GH secretion and
re-emphasises the importance of anthropometric data in disting-
uishing those children who will respond to GH therapy.

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LOW DOSE TESTOSTERONE TREATMENT OF DELAYED GROWTH.

Anabolic steroids are used to accelerate the
growth of normal boys with constitutional delay of
growth and puberty. We have treated 17 healthy boys aged 9.8 to
15.9 years (mean 13.3 years) who were short (height SDS -1.6 to
-4.7, mean -2.9) and had bone ages ≥2 years below chronological
ages with low-dose testosterone enanthate, 0.8-1.2 mg/kg i.m.
monthly, for 0.9 to 2.8 years. This increased their height
velocity by 3.9 ±1.2 cm/year (mean±SD). During the therapy their
bone age advanced 1.5 years/year (mean) and the mean change of
RWT height prediction was +1.1 cm, but the individual variation
was wide. Those 6 whose final height is known by now have all
ended up within 3 cm of their initial RWT prediction. The signs
of puberty advanced slowly: of those 10 with no signs of puberty
initially,5 remained so after 6 months,and 1 after 1 year. The
acceleration of growth and puberty induced by testosterone was
not statistically significantly different from that seen in a
group of 13 similar boys treated by us earlier with fluoxyme-
sterone 0.1 mg/kg daily (Acta Pediatr Scand 1982;71:929).
Testosterone enanthate has the advantage over fluoxymesterone
that it is more physiological, and needs to be taken only monthly
so that the boy does not get a daily reminder of the inadequacy
of his growth and pubertal development.

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COMPARISON OF EXERCISE TESTING AND 24-HOUR GROWTH
HORMONE SECRETION IN 42 CHILDREN WITH GROWTH RETARDA-
TION.

At the present time, investigations of physiological growth hormone (GH) secre-
tion are preferred to pharmacological tests. We compared two of the former methods,
study of 24-hour GH secretion and exercise testing, in order to clarify their res-
pective usefulness. We studied 42 children (30 boys and 12 girls) with growth re-
tardation (mean = - 3.07 ± 0.9 SD) whose mean age was 12 yr 4mo ± 4 yr 2mo.
Thirty-three were at pubertal stage P1 and nine P2. Exercise testing was carried
out using an ergometric bicycle and we sought to obtain maximum effort (maximum
VO2, respiratory quotient, heart rate). Sampling was done during the 20 min after
the test. Study of 24-hour GH secretion was carried out with sampling every 20 min
and the integrated concentration (IC), number of peaks and maximum peak were cal-
culated. Two groups were analysed :
– Group I (n = 31) children who had reached maximum effort. Among these
children : 24 had normal GH secretion (IC > 3 ng/ml and maximum peak > 10 ng/ml),
10 had a normal response to exercise testing (peak > 10 ng/ml) and 9 response <
10 ng/ml; 6 had low 24-hour GH secretion and all these 6 had a secretory peak <
10 ng/ml in response to exercise.
– Group II (n = 11) children who had reached submaximum effort. None of these
children had a GH secretory peak > 10 ng/ml in response to exercise, whereas
24-hour GH secretion was normal in 8/11.
In conclusion, these results show that exercise testing cannot be considered
a reliable method of investigation of GH secretion. If effort is submaximum, the
percentage of false negatives is 100 % and when effort is maximum there are 36 %
false negatives.

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SHORT TERM TESTOSTERONE (T) TREATMENT AT A PERIPU-
BERTAL BONE AGE (BA) DOES NOT REDUCE ADULT HEIGHT
(AH) IN BOYS WITH CONSTITUTIONAL DELAY (CD).

Growth data and AH from 22 untreated patients with CD (group
1) were compared retrospectively with those of 19 patients, who
had received long-acting T-esters (100 to 250 mg per month, mean
total dosage 1029 mg/m2) during 2 months to 3.25 yrs (mean dura-
ion 8.5 months, group 2). Age (group 1 15.4+/-1.2 yrs, group 2
16.2+/-1.4 yrs), BA (group 1 12.6+/-1.3 yrs, group 2 13.1+/-1.2
yrs) at first examination (group 1) or start of treatment (group
2), and AH (172.8+/-7.5 cm group 1, 176.8+/-8.0 cm group 2) were
not significantly different and corresponded to target height
(172.6+/-5.9 cm group 1,176.8+/-4.7 cm group 2).In group 2,there
was no negative correlation between total T dose and AH, and the
latter corresponded to predicted height (175.7+/-6.4 cm Bayley &
Pinneau, 178.8+/-8.1 cm Roche et al., 173.9+/-6.4 cm Tanner et
al.) in the same way, as in the untreated patients (175.1+/-8.1,
171.6+/-5.9,and 170.8+/-5.7 cm respectively).It is concluded that
temporary treatment with long-acting T-esters (100 to 250 mg per
month during 6 months, starting at a BA above 12.5 years), which
has positive psychosocial and physical effects, does not have any
negative somatic consequences and does not reduce AH in boys with
CD.This simple and economical treatment will thus not be obsolete
with recombinant hGH available in large quantities.It has the ad-
vantage of stimulating not only growth velocity,but also physical
strength and development of the secondary sex characteristics.