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## 113 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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## 114 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/l) to pharmacological stimuli of either glucagon, clonidine or insulin induced hypoglycaemia; mean peak GH attained to pharmacological stimuli was 27.5 mU/l (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 distinguishing those children who will respond to GH therapy.

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## 115 COMPARISON OF EXERCISE TESTING AND 24-HOUR GROWTH HORMONE SECRETION IN 42 CHILDREN WITH GROWTH RETARDATION.

At the present time, investigations of physiological growth hormone (GH) secretion 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 respective usefulness. We studied 42 children (30 boys and 12 girls) with growth retardation (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 $VO_2$, 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 calculated. 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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## 116 ADVANTAGES OF THE hGH 24hr SECRETORY PATTERN IN DISTINGUISHING GROWTH DISORDERS.

We performed a comparative study of 24hr hGH secretion vs. stimulation tests in 48 pts. (29M, 19F) with growth disorders, divided 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 | Age 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 rhythmicity were observed by cosinor and power spectra analysis. The present study indicates that the analysis of the hGH 24hr secretory pattern is a more sensitive discriminator of the GH-RH-hGH axis than provocative tests.

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## 117 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 fluoxymesterone 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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## 118 SHORT TERM TESTOSTERONE (T) TREATMENT AT A PERIPUBERTAL 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 duration 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 advantage of stimulating not only growth velocity,but also physical strength and development of the secondary sex characteristics.