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Classification of patients with GH deficiency (GHD) according to the response to GH-RH

Synthetic GH-RH-1-44 was administered in a dose of 1 mcg/1 Kg to 3 normal adolescents with short stature and to 17 patients with GHD (hGH response to ITT and clonidine < 2 ng/ml). In the normal subjects the peak response of plasma hGH to GH-RH was 100, 20 and 19 ng/ml. In the GHD patients 3 patterns of response were observed: a) Good response (n=5), 18±1.9 ng/ml, i.e. GHD of hypothalamic origin; b) Partial response (n=4), 4.25±0.4 ng/ml, i.e. GHD of hypothalamic origin, possibly with a pituitary component; c) No response (n=8), 1.3±0.3 ng/ml, i.e. GHD of pituitary origin. It remains to be established whether a partial response of GH to one bolus of GH-RH may in certain patients be due to a long-standing GH-RH deficiency, with the possibility of its unmasking following repeated injections and the consequent synthesis of sufficient GH for its release.

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Comparison of spontaneous GH secretion during daytime and during sleep in children with short stature.

Daytime (0.800H-20.30H) growth hormone (GH) secretion was studied in 24 children (18 boys, 6 girls, of mean age 12 years 6 months ± 3 years 6 months) with short stature (m=3.5± 1.3 SD), and was compared with GH secretion during sleep using a polygraphic monitoring (EEG, EMG, EOG). The results of pharmacological tests allow two groups to be distinguished: 1) A first group (n=12) of normal responders (peak > 10ng/ml): the study of daytime secretion clearly demonstrates spontaneous pulses (m=1.4) of mean duration 70minutes. The mean of these peaks is 20.5±7,8 ng/ml.The study of GH secretion during sleep was carried out in six cases and is inagreement with the daytime secretion. 2) A second group (n=12) of partial deficiencies (peak<10ng/ml after two pharmacological tests): the study of daytime GH secretion revealed only one case of a peak > 10 ng/ml. The study of GH secretion during sleep, carried out on all cases, showed a response < 10ng/ml in 4 cases and a response > 10ng/ml in 8 cases. In this group, therefore, a discordance exists in 7 out of 8 cases: low response of daily secretion and normal response during sleep. These results allow us to demonstrate the existence of spontaneous secretion of GH during the daytime as well as the absence of concordance between this result and GH secretion during sleep in partial GH deficiencies.There is also in this group an extremely high percentage of false negatives (bad responders for daytime GH secretion).

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Growth response for growth hormone/GH/replacement therapy: Serum 1,25 dihydroxy vitamin D/1,25/OH/$_2$D/increment.

Increased calcium and phosphate bone turnover in rapidly growing patients requires an augumentation in the intestinal calcium absorption which depends on 1,25/OH/$_2$D. Catch up growth in the GH treated patients is therefore supposed to be a status which requires an increase of 1,25/OH/$_2$D generation. To test this supposition we estimated serum 1,25/OH/$_2$D in 22 pituitary dwarfs before and during growth spurt. The blood samples were collected before GH treatment, 11 days and 7 to 8 weeks after the replacement therapy was instituted. The significant raise in 1,25/OH/$_2$D serum level during therapy was observed /20.8±8.0, 31.7±15.3, 34.1±17.0 pg/ml respectively/. This was more pronounced in children with less advanced skeletal maturation, lower stature and with better growth response to the replacement therapy. The 1,25/OH/$_2$D serum concentration was not related to the prolactin level and to the deficiency of other pituitary hormones neither before nor after GH treatment.

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Oxandrolone and spontaneous hGH-secretion

The effect of oxandrolone (Ox) on the spontaneous hGH-secretion was studied in 6 prepubertal children diagnosed as constitutional delay of growth and adolescence (CD). The spontaneous secretion pattern of hGH during a 24hrs. period was analysed before and after a 5-8 weeks therapy with Ox, 1.o mg/kg daily. Blood samples were taken in 6o min. intervalls. All patients had well documented sleeping phases during night. For evaluation we looked for the integrated hGH-concentrations (ng x min x ml^{-1};(1)) as a parameter for the total secretion per day, the 3 maximal peak values and the number of secretion periods. Results: Comparing the hGH-secretion pattern before and after Ox (Wilcoxon-test, 95% confidence level), no differences were proven regarding the criteria mentioned.Conclusion: Ox does not stimulate the spontaneous hGH-secretion in patients with CD and may exert its growth promoting activity in another way.

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Effect of growth hormone releasing factor (GRF) on serum growth hormone (GH) and prolactin (PRL) in hypopituitary children.

GRF may be of value in investigating growth disorders. An IV bolus of 0.5 µg/kg of GRF-44-NH_2 (Peninsula Labs, USA) was given to 12 short normal children (N) and 24 children with documented GH deficiency (GHD). Serum GH and PRL were measured by RIA. In the N group, GRF induced a rapid and ample GH response :

Time (min)	-30	0	5	10	15	30	45	60	90	120	150	180
Mean GH	2.8	2.8	22.8	27.5	29.4	21.3	13.7	10.1	8.4	5.8	3.5	2.7
SEM (ng/ml)	0.8	0.9	5.4	5.7	3.4	5.1	4.0	3.4	3.9	1.1	0.7	0.8

In the GHD group, mean peak GH after GRF was lower than in the N group (8.0±2.5 vs 39.2±5.1 ng/ml, p<0.001) but peaks within the normal range were seen in the youngest GHD patients. In the N group, PRL decreased continuously over the 3 hours of the test, a reflection of its normal circadian rythm (222±54 at 9 AM vs 108±27 µU/ml at 12 AM, p<0.05). In 7 GHD patients, PRL peaked 15 minutes after GRF (366±73 at 0 min vs 494±85 µU/ml at 15 min, p<0.05); in 2 patients with genetic GHD, PRL decreased to a nadir at 60 min, followed by a rebound; in the remainder of the GHD group there was no change in PRL. Conclusion : 1) GRF at a dose of 0.5 µg/kg is a potent GH secretagogue in children; 2) Some GHD children have GH responses to GRF within the normal range; 3) The PRL response to GRF in GHD is heterogeneous.

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Long-term studies of effects of methionyl-human growth hormone in hypopituitary patients.

Ten children with growth hormone deficiency (GHD), were included in a clinical trial with methionyl-human growth hormone (M-hGH). Six of them (A) previously treated with human growth hormone (hGH) were switched to a 9 months double-blind study with the same dosage (4 I.U./3 times a week) of M-hGH or hGH and the four new cases (B) received an equal dosage of M-hGH for 6-9 months. The patients were clinically controlled every 3 months. Growth hormone antibody titre (GHA) was determined every 1 1/2 months and bioassayable somatomedin (BSM), somatomedin C (SMC) and other biochemical parameters every 3 months. Results : 1- Growth velocity was maintained at previous values in A in all cases and in B a clear catch-up was observed. 2- Both treatments normalized BSM levels throughout the study but wide variations in SMC were observed. 3- Antibody titre was positive at 3-6 months in the majority of cases treated with M-hGH, with a progressive increase of GH basal levels. In conclusion : M-hGH induces generation of BSM and promotes growth in GHD, but more prolonged study on the characterization and possible side-effects of GHA is required.