39 EFFICIENCY OF GROWTH PROMOTING ACTION OF hGH IS HIGHEST IN VERY YOUNG DEFICIENT CHILDREN.

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The effect of hGH treatment was studied in 21 prepubertal (12 M, 9 F) GH deficient children (14 IGHD, 7 MPHD) treated for 5 yrs. They were grouped according to age at start of therapy: Gr. A: CA 0.9-4.8, BA 1±1 y; Gr. B: CA 5.1-9.9, BA 3.8±2 y. The initial dose of hGH was 2-4 IUx3/wk.

Gr.			Before	Years of Treatment 1	2	3	4	5
A	11	CA (yr)	2.7±1	3.7±1	4.7±1	5.7±1	6.7±1	7.7±1
		Ht vel (cm/yr)	6.1±3	12.0±3	8.3±2	7.2±2	7.2±2	7.0±1
		Ht SDS	-5.2±1	-3.7±1	-2.9±1	-2.7±1	-2.2±1	-1.9±1
B	10	CA (yr)	7.4±1	8.4±1	9.4±1	10.4±1	11.4±1	12.4±1
		Ht vel (cm/yr)	4.0±2	9.0±1	5.7±2	4.8±1	4.9±1	4.4±1
		Ht SDS	-3.7±1	-2.8±1	-2.7±1	-2.8±1	-2.5±1	-2.6±1

In Gr. A the mean height SDS gain in the first year was 1.5 compared to 0.8 in Gr. B. In the 2nd year height SDS gain was 0.8 and 0.2 respectively. The SDS gains decreased with years of therapy. The bone age advancement was faster in Gr. B. It is concluded that initiation of hGH therapy in early age is most effective for height normalization, especially in isolated hGH deficiency.

40 hGH RESPONSE TO GH-RH 1-44 IN OBESITY OF VARIOUS ETIOLOGIES.

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Fourteen juveniles with obesity were tested with i.v. GH-RH 1-44 (1 mcg/kg). Seven had simple obesity and in the other 7 the obesity was associated with the following syndromes: Prader-Willi (n=4); Laurence Moon Biedle (n=1); hypothalamic syndrome (n=2). The overweight (Owt) SDS was calculated by substracting height SDS from weight SDS. The subjects were grouped according to the diagnosis and Owt SDS (Table). In simple obesity (Gr. 1+2) there was a good response of hGH to GH-RH (11.8±5.8 ng/ml) whereas in the syndromes (Gr. 3+4) there was a poor response (3.2±2.1 ng/ml $p < 0.01$). In groups 2 & 3 there was a similar Owt SDS, but different etiologies of the obesity with a significantly reduced hGH response in the syndromes (Gr. 3; $p < 0.01$). Though the blunted response of hGH to pharmacologic stimuli as well as to sleep and GH-RH in obesity is related to the degree of Owt, it is concluded that additional factors contribute to the pattern of hGH secretion and response in obesity.

Group	n	Age y:m m ± SD	Owt SDS m ± SD	Peak hGH ng/ml m ± SD
1 Simple obesity	4	12:5±1:3	2.5±0.7	10.9±6.1
2 Simple obesity	3	13:2±3:0	5.4±0.7	12.9±6.2
3 Syndromes	4	11:0±5:2	4.2±0.4	3.3±0.3
4 Syndromes	3	13:0±6:4	7.6±1.5	3.1±3.6

41 EUROPEAN COLLABORATIVE STUDY ON THE EFFECT OF SYNTHETIC I-44 GROWTH-HORMONE-RELEASING-FACTOR(GRF) ON PLASMA GROWTH HORMONE(GH) IN PREPUBERTAL CHILDREN WITH GROWTH FAILURE. (GRF European Multicenter Study).To be presented (if accepted) by Pierre Chatelain. INSERM U.34.LYON.FRANCE

A 27 European centers collaborative study (supported by SANOFI.) was undertaken to assess the effect of a 2µg/kg/body weight I.V. bolus of synthetic I-44 GRF(SANOFI.) on plasma immunoreactive GH in children w-th growth failure. I06 among the first I06 tested (further analysis extended to 500), in strict compliance with the protocole according to an independent Validation Committee (V.C.) were accepted and classified as: A= no GH deficiency(n=49),B=partial GH deficiency(n=23),C=total GH deficiency(n=34) according to a GH peak(mUI/ml) above 20(A),between I9.9 and 10.I(B) or below I0(C) assessed by I or 2 conventional GH secretion provocative tests prior to GRF. The likely cause of growth failure was CNS disorder (n=22), Idiopathic GH deficiency (IGHD, n=38), Chronic disease (n=6), Constitutional short stature (n=40). Mean GH peak (mUI/ml) after GRF were 48.8(A), 32.6(B) and 16.4(C) at 45', 30' and 60' respectively. In partial(B) or total(C) IGHD, mean GH peak (mUI/ml) were 35.8 and 14.9. A good relationship between the GH response to grf and the bio-clinical diagnostic classifisation established by the V.C. was observed. I2/34 patients of C displayed an improved GH response after GRF, previosuly underestimated by other secretagogues. GRF proves to be a well tolerated,usefull and non invasive mean in the assessment of GF secretion in growth deficient children.

42 EFFECT OF ACUTE I.V. GROWTH HORMONE-RELEASING-FACTOR (GRF) ON PLASMA PROLACTIN(Prl) IN GROWTH HORMONE(GH) DEFICIENT PATIENTS.

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54 patients (43 children) with GH deficiency documented by 2 GH secretion provocative tests (peak 5ng/ml) were given Iµg/kg/b.w. I.V. bolus of synthetic I-44 GRF (Generous gift from R.Guillemin, the salk Institut). Plasma GH and Prl were assayed from time O'to I20 GH deficiency was Idiopathic(IGHD.n=24)or secondary to a brain tumor (TGHD.n=30). I6 patients (7/24 IGHD+9/30 TGHD) displayed basal (B) hyperprolactinemia (Prl 450mUI/l).

MEANS	B.Prl(mUI/l)	GH(ng/ml)	Prl
HYPER B.Prl(n=I6)	776.9	9.6	238.8
NORM. B.Prl(n=38)	I96.4	I5.6	I48.I

The only positive correlations found were between Basal Prl and Prl, specially among B.hyperprolactinemics ($r=0.62$-p 0.005). Surprisingly no correlation was found in any group between B.Prl and GH nor Prl and GH. Some subjects displayed a Prl peak with no GH peak, others a GH peak and no Prl peak. This study confirms that GRF can induce a Prl rise. Vascular flush is not the only possible explanation. A Prl peak with no GH response suggests that GRF had reached the pituitary and non functionnal or atrophic Somatotrophs. Chronic GRF stimulation may be required to maintain or induce functionnal Somatotrophs. In GH deficiency. B.hyper-Prl cannot predict GH response to GRF. Asinle GRF injection cannot exclude GRF deficit.Prl is worthwile assaying after GRF.

43 SHORT STATURE AND CELIAC DISEASE: CAN THE SIMPLE DETECTION OF THE ANTIBODIES TO GLIADIN RESOLVE THIS RELATIONSHIP?

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107 nonselected children (77 m. and 30 f.) with short stature and absence of gastrointestinal tract symptoms were examined. In addition to the normal tests for the pathogenetic definition of short stature, in all patients a duodenal biopsy was performed and antibodies to gliadin were detected (immunofluorescence (IFL-AGA) and a micro-ELISA method (ELISA-AGA)) We found 8 children (7.5%) with total villous atrophy probably due to celiac disease, 7 children (6.5%) with partial villous atrophy, and 4 children (3.7%) with complete GH deficiency. IFL-AGA were found in 17 (15.9%) cases: in all the 8 (100%) children with total villous atrophy, in 3 (42.8%) children with partial villous atrophy, and in 6 (6.5%) short normal children. ELISA-AGA were detected in: 7 (87.5%) of the 8 children with total villous atrophy, in 4 (57.1%) patients with partial villous atrophy, in 1 (25%) patient with complete GH deficiency, and in 9 (9.8%) short normal children. These two tests were discordant in: 1 case of total villous atrophy, 1 case of partial villous atrophy, 1 case of complete GH deficiency and in 3 cases of short normal children. IFL-AGA therefore, seem to be able to detect all the cases with total villous atrophy (probable celiac disease), while its significance in the cases with partial villous atrophy is not yet clear. The same test gives an acceptable percentage (6.5%) of certainly false positivity. ELISA-AGA appear to be less specific. In conclusion, the relationship between short stature and celiac disease seems to be clearly resolvable by means of a simple detection of the IFL-AGA.

44 GH, HPRL, ACTH, TSH AND SmC RESPONSE TO GH-RF IN CHILDREN WITH PITUITARY DWARFISM.

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20 prepubertal GH-deficient children (C.A. 4.88-17.75yrs) were studied; 15 patients had isolated GH-deficiency, 5 had multiple pituitary hormone deficiencies, such as GH-ACTH-TSH (1 case), GH-TSH (2 cases), GH-LH-FSH-TSH (1 case) and GH-LH-FSH (1 case). In all patients synthetic human GH-RF (1-40) was administered i.v. at a dose of 3 µg/Kg at time 0 and blood samples for GH and HPRL were taken at -15,0,15,30,45,60,90,120 and 180 min; samples for TSH and ACTH were taken at 0,30,60,90 and 120 min, and for SmC at 0,30,60,120 and 180 min after injection. A significant GH-response (≥ 4ng/ml) was attained in 13 patients (11 with isolated GH-deficiency and 2 with multiple hormone deficiencies); GH levels increased at 15 min and reached a peak at 30 min. In these patients a significant increase in HPRL levels was observed after 15-30 min. In the whole group there were no changes in ACTH, TSH and SmC levels. The 7 patients who did not respond to GH-RF were not different with regards to age, sex, duration of treatment and response to the latter, from those who did respond. In our study a hypothalamic deficiency was present in 65% of the subjects. These data suggest that GH-RF could be useful in the treatment of a high percentage of GH-deficient patients.