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SINGLE AND MULTIPLE PULSES OF GROWTH HORMONE (GH) IN THE TREATMENT OF GH DEFICIENCY

We have compared subcutaneous (s.c.) pulsed administration of hGH 0.6 IU 3 hourly at night with hGH 2 IU administered s.c. and 4 IU administered i.m. in 6 GH deficient children aged 5.9-11.6 years. Five had received hGH 4 IU i.m. for 3.6 years (range 2.5-4). Each of these children and one new patient received hGH 2 IU s.c. and 0.6 IU 3 times each night via a mini infusion pump for 6 months in random order. Serum GH profiles were obtained on all treatment regimens.

Peak GH concentrations and areas under the GH curves were dose related. The time to attain the GH peaks was similar using i.m. (3.6h) or s.c. (3.9h) routes. A single injection did not mimic physiological GH pulses but these were more closely attained using pulsed administration.

Four children completed the entire study; 3 grew equally at all times but height velocity fell in one on the pulsed regimen. Following cessation of all GH treatment, mean height velocity SDS (-4.0) was significantly lower than before all treatments (-2.1).

Pulsatile hGH administration is effective but had no significant advantage. A post treatment velocity must not be used to measure the effects of a treatment.

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FINAL HEIGHT IN 22 PATIENTS WITH IDIOPATHIC GROWTH HORMONE (GH) DEFICIENCY AFTER LONG TERM TREATMENT WITH GH

The aim of this study was the evaluation of final height in patients treated with GH and to examine whether any auxological, hormonal or therapeutic factors have a significant influence on the result. 22 patients with idiopathic total GH deficiency were studied, 8 had isolated GH deficiency, 14 had various additional pituitary deficiencies. At the onset of treatment CA was 10,1±4 yrs (x ± SD), BA -4,7 ±1,8 SDS, height -4,7±1,2 SDS_{CA} and -0,54±1,5 SDS_{BA}. Duration of GH therapy was 6,6±3 yrs, the average weekly dose was 9,1 ± 2,0 U. Final height was significantly correlated with target height ($p<0,001$). If final height was expressed in SDS of target height, there was a significant correlation with the height SDS_{BA} ($p<0,01$) at the onset of therapy. No correlation between final height and height SDS_{CA}, CA, BA, weight SDS for height, respectively at the onset of treatment or stimulated GH levels, serum SM-C, growth velocity during the first year or GH dose or duration of GH treatment could be found. In addition, patients were arbitrarily classified in two groups, one with a mean final height of -1,3±0,8 SDS_{CA} (n=12, group A) and one with final height of -3,7±0,6 SDS_{CA} (n=10, group B). The groups did not differ in any of the encountered parameters. However, in group A 9/12 patients (vs.1/10 in group B) had additional gonadotropin deficiency ($p<0,01$). In conclusion, parental height and height for BA at the onset of treatment seems to have an influence of final height. Patients with additional gonadotropin deficiency had a better prognosis.

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HEAD AND BODY MEASUREMENTS IN PATIENTS WITH IDIOPATHIC GROWTH HORMONE DEFICIENCY (IGHD)

In a previous anthropometric study, Zachman et al. (1980) showed that GH deficient children had characteristic differences in cranial proportions and less retardation in head growth compared to stature and other body dimensions.

To extend these results 15 head and 12 body measurements were taken on 83 patients (27 girls of mean bone age 1.5 - 11.0 "years", mean 6.0 "years"; 56 boys of mean bone age 1.0 - 13.5 "years", mean 5.1 "years" with isolated GH deficiency. These were compared with a large population of normal Polish children of the same age or height. All measurements were expressed as standard deviation scores (SDS). The mean stature of the girls was -4.8 ± 1.2 SDS and for boys -4.8 ± 1.8 SDS. Our data showed that all face measurements, along with occipital breadth, were disproportionately small in the GH deficient children compared to children of the same height. In contrast head breadth, length and circumference were not different although forehead breadth tended to be greater. There was no disproportion between head breadth and length.

In girls only, the mean biacromial SDS was significantly less than that for biiliocristal diameter.

We conclude that growth of the bones of the face and the skull base it more retarded than that of the cranial vault or long bones which gives rise to the classical clinical facial characteristics of the GH deficient child.

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CONGENITAL GROWTH HORMONE DEFICIENCY (cGH-D) ASSOCIATED WITH MICROPENIS: A "TRANSITORY ANDROGEN INSENSITIVITY SYNDROME ?"

Androgen receptor analyses of scrotal skin from a boy with cGH-D associated with micropenis, done at age 1 and 3 yrs, respectively, revealed decreased cytosolic binding for testosterone(T) and dihydrotestosterone (DHT), compared to age matched controls. Rises in serum androgens (ΔF) after hCG-stimulation as well as androgen-5α-reductase (A5R) activities were also evaluated at both ages.

Pat. P.M.	cytosol - (RECEPTOR) - nuclear				A5R	ΔF
	T	DHT	T	DHT		T-DHT
	Kd[nM]/Nmax[fM/mg]				[pM/h.mg]	
1 yr	1.05/28	1.56/30	ND	0.70/117	3.20	3.07-1.25
3 yrs	1.00/25	1.30/114	6.00/90	1.04/180	16.10	6.06-1.50
controls (mean values)						
1 yr	2.09/150	1.52/205	2.10/25	1.33/91	(15.80)	
3 yrs	2.33/130	1.29/480	1.21/22	1.30/181		

Stretched penile length was 1.1 cm (P3) at age 1 and increased up to 3.2 cm (P25) at age 3. body length followed the P3 under treatment with synthetic GH. The receptor and A5R data are in agreement with the development of the external genital status and indicate a "catch-up" growth of the sexual development. From the clinical observations in combination with the laboratory findings presented here, a "transitory androgen insensitivity" might be postulated.

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THE ASSOCIATION OF THE EMPTY SELLA SYNDROME WITH ADVERSE PERINATAL EVENTS IN IDIOPATHIC GROWTH HORMONE DEFICIENCY.

In order to study structure function relationships of the pituitary in growth hormone deficiency (HGD) high resolution computer assisted tomography (HR-CAT) was performed in 24 consecutive children with idiopathic GHD. The population studied was characterised thus: 11 male, 13 female; age range newborn to 15 years; 15 isolated GHD, 9 multiple pituitary hormone deficiency (MPHD); 17 sporadic and 7 familial GHD; 11 had recorded adverse perinatal events (breech or forceps delivery, asphyxia, excessive bruising, surfactant deficiency, exchange transfusion, umbilical haemorrhage and neonatal fits); 19 had iv growth hormone releasing factor tests ($hp\text{-}GRF_{1\text{-}44}$) at diagnosis.

HR-CAT scans showed 13 children to have an empty sella and 3 with a partially empty sella - Group 1; and 8 with a full sella - Group II. No difference between Group I and II was found with respect to: Age, sex or auxology at presentation; isolated GHD or MPHD; sporadic or familial GHD; growth hormone response to GRF. However, perinatal adverse events were strongly associated with Group I ($p = 0.02$).

The present findings support the concept that adverse perinatal events are a major factor in the aetiology of GHD - possibly by compromising the blood supply to the pituitary.

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EXAMINATION OF THE AUXOLOGICAL AND HORMONAL PARAMETERS IN 100"SHORT NORMAL" RE: DIAGNOSIS OF "SUSPECTED GH DEFICIENCY".

100 subjects, 3rd percentile for height, were submitted to three tests; sleep (8 pm-7.30 am), arginine and L-dopa. Patients: 75 males (a. 5.7/16.2), 25 females (a. 4.8/14.1). All subjects had a normal peak >8ng/ml in the sleep test. 24 had a normal peak in 1 pharmacological test (group A), 13 had a norm. peak in 2 pharmac. tests (group B) and 63 had no peak in 2 pharmac. tests (group C). In puberty the percentage of group A and B was signific.higher than in prepuberty. The 3 groups were compared as regards growth and endocrinological data (height SDS, bone age, bone age SDS, height velocity SDS, GH Mx peak and area in sleep test, SmC 8 am and 8 pm). All the data were similar except HV SDS, lower in group C ($P<0.05$ vs B, $P<0.01$ vs A). If patients are separated as SmC 8 am (<10th perc. or >10th perc. for age; our data for normality), the percentage of 3 groups is similar in two ranges of SmC. There was no correlation between data of sleep test and data of pharmacological tests. The examination of GH in sleep test (peak mx, area), indicated: 1) mx peak was higher in prepubertal males ($P<0.05$), and in these the area was higher in subjects without bone age delay($P<0.001$); 2) the data of subjects with GH area <mean -1 SD were similar to the subjects with area >mean +1 SD; 3) no correlation between GH area and SmC (correlation SmC-bone age was excluded). The examination of SmC indicated: 1) SmC is correlated with bone age only in males ($P<0.025$); 2) SmC is higher in puberty ($P<0.05$); 3) Pubertal males with SmC <10th perc. have lower area than subjects with SmC >10th perc. ($P<0.05$);