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EFFICACY OF BIOSYNTHETIC HUMAN GROWTH HORMONE (BIO-HGH) IN STIMULATING GROWTH IN PREPUBERTAL (PRE) AND PUBERTAL (PUB) CHILDREN WITH GROWTH HORMONE DEFICIENCY (GHD)

In an open, prospective, non-comparative study, 37 previously treated (PrTr) (with extracted HGH) and 5 previously untreated (PrUn) GHD children (height (Ht) < 3 percentile or Ht velocity (Vel) < 4 cm/year; max.serum-GH < 10 ng/ml in at least two standard stimulation tests) were given Bio-HGH (Somatropin-Lilly) s.c.0.06 mg/kg three times a week to a max. of 8 mg per week. Treatment with Bio-HGH began at least 5 months after treatment with extracted HGH had ceased. Height was measured within 2 months after previous treatment was discontinued. Lower leg length (LLL) measurements were started 6 weeks before treatment with Bio-HGH by using a knemometer. Ht Vel (cm/yr) and LLL Vel (mm/yr) are shown in the table (mean±SD).

		Before Bio-HGH		13 weeks Bio-HGH	
Group	n	LLL Vel	Ht Vel	LLL Vel	Ht Vel
PrUn Pre	5	14.3± 6.0	3.2± 2.0	35.0± 9.5	10.0± 3.2
PrTr Pre	24	11.1± 8.2	1.4± 1.9	33.6± 8.0	9.4± 2.5
Pub	13	9.8±10.2	2.6± 2.5	25.3± 8.9	8.2± 2.7

LLL Vel correlated more significantly with Ht Vel during (r=0.75) than before (r=0.47) Bio-HGH treatment. Because LLL was measured only 6 weeks before Bio-HGH was started, the LLL Vel probably reflects more accurately the efficacy of Bio-HGH in PrTr patients.

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CLINICAL STUDIES IN GROWTH HORMONE DEFICIENT PATIENTS (GHDP) USING DIFFERENT PREPARATIONS OF 192-RECOMBINANT HUMAN GROWTH HORMONE (192-rhGH), SI, SII, SIII, ACCORDING TO THEIR E.COLI PROTEIN CONCENTRATION (ECPC).

192-rhGH (Somatrem) with ECPC of 285-1400 (SI), 170-30 (SII) and <10 (SIII)/ng/vial was used in 3 studies in GHDP not previously ("new") or previously ("old") treated with pit-hGH. In 8 "old" patients (duration 1 month (m)), glucose and insulin responses in the OGTT, insulin binding in erythrocytes and somatomedin activity (SMA) were similar on pit-hGH or SI. Absence of hGH-antibodies (hGH-ab) during this period. On SII (9 patients, duration 9-12 m.) and SIII (21 patients, planned duration 1 year, results presented of 6 m), "new" patients experimented typical catch-up growth and the old ones maintained their previous growth velocity (g.v.). SMA correlated with g.v. and adult height prognosis improved throughout treatment. hGH-ab test was positive on SII at 3 m. of treatment in 77% of cases and in 88% at 9-12 m., while on SIII at 3 m. and 6 m. hGH-ab test was positive in only 8% and 16% of cases not previously treated with SII but again in 88% of patients previously treated with SII. Binding capacity of hGH-ab was very low. ECP-ab were already positive in 33% at onset and increased moderately later. Thus 192-rhGH promotes g.v. and SMA and, as in the majority of cases hGH-ab test is already positive at 3 m., SIII is clearly less antigenic than SII. Patients previously treated with SII possibly developed an anamnestic response on SIII. No other side effects were observed.

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COMPARISON OF THE LIPOLYTIC POTENCY OF PITUITARY-DERIVED AND BIOSYNTHETIC GROWTH HORMONE IN HYPOPITUITARY CHILDREN.

Whether lipolysis is an intrinsic property of the growth hormone (GH) molecule or is due to contaminants of pituitary origin remains controversial. We therefore compared the rise in plasma free fatty acid (FFA) levels measured with the Nefa Quick "BMY" kit, Boehringer) induced by either pituitary GH (pit-GH, Nanormon, Nordisk) or biosynthetic GH (syn-GH, Somatonorm, Kabi) in 34 hypopituitary children (age 5 - 18 years, peak plasma GH < 5 ng/ml after insulin and glucagon tolerance tests). The patients were admitted after an overnight fast and fasted until 1230 hr on both study days. On day 1, no injection was given. On day 2, 0.2 U/kg of either pit-GH (N=5, group A) or syn-GH (N=29, group B) was given IM at 0830 hr. The FFA levels at 1230 hr are expressed as % of the 0830 hr value. In group A, mean (± SEM) plasma FFA levels at 1230 hr were 138.7 ± 9.8 % of the 0830 hr value on day 1 and 233.1 ± 20.0 % on day 2. In group B, they were 130.3 ± 10.9 % and 267 ± 22.6 % on days 1 and 2, respectively. Thus, both GH preparations induced a rise in plasma FFA levels greater than that induced by fasting alone ($p < 0.001$) but the two GH preparations were not significantly different from each other ($p > 0.2$). We conclude that the acute lipolytic effect probably represents an intrinsic property of the GH molecule.

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SEX DIFFERENCES IN GONADAL ESTRADIOL (E2) AND ESTRONE (E1) CONCENTRATIONS IN INFANCY

To clarify the origin of estrogens in infant blood, we measured E1 and E2 in the gonads of 50 girls and 64 boys deceased by sudden death between birth and 2 years of age. In both sexes, E2 was the major gonadal estrogen which exceeded E1 almost tenfold in the ovaries and twice in the testes. Thus, there was a clear sex difference in gonadal estrogen concentrations. On an average, girls had 8 times higher E2 and twice as high E1 concentrations in their gonads than boys. As in plasma, E2 concentrations were highest in ovaries of 2 to 4 months old girls (2 - 55 ng/g) and in testes of 1 to 3 months old boys (0.6 - 6.4 ng/g). Ovarian E2 concentrations decreased to values below 3 ng/g until the end of the 1st year of life, testicular E2 reached values below 1 ng/g already by 6 months of age. The gonadal steroidogenic activity paralleled changes in gonadal morphology. Ovarian weights showed a similar pattern of rise and fall as the E2 concentrations, the biggest ovaries consisting of multiple macroscopic cysts. In boys, testicular E2 closely correlated with Leydig cell development and testicular testosterone concentrations. We conclude that the surge of E2 in the blood of infant girls and boys originates from ovarian follicles and testicular Leydig cells, respectively, which develop under the influence of the characteristic post-natal gonadotropin surge.