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GROWTH HORMONE AND ESTROGENS IN PATIENTS WITH TURNER SYNDROME: *IN VIVO* AND *IN VITRO* STUDIES. D. Larizza*, A. Barreca°, P. Ponzani°, G. Damonte°, F. Lo Curto^, F. Minuto", F. Severi*, G. Giordano°, *Clinica Pediatrica, Università di Pavia, Cattedre di °Endocrinologia e di "Fisiopatologia Endocrina, DISEM, Università di Genova, ^Biologia generale e Genetica Medica, Università di Pavia, Italia.

We studied the effect of GH alone (1U/Kg/week s.c.; 20 pts) and in combination with ethynyl estradiol (EE; 50 ng/kg/die per os; 6 pts) on IGF-I and II plasma concentrations in age-matched (M±ES: CA 11.29±0.38 and 11.95±0.94, BA 9.97±0.55 and 9.95±0.93) pts presenting with TS and on the IGF-I generation by fibroblasts in culture from 3 TS pts and 1 control. IGF-II plasma concentration was normal and unresponsive to the treatment. IGF-I plasma basal concentration was normal and increased significantly in both groups after 12 months of treatment. No difference was found between the two treatment regimens. Furthermore, we verified the ability of the fibroblasts from TS pts to synthetize *in vitro* the IGF-I in basal and GH, EE or GH + EE stimulated conditions. The results indicate that TS fibroblasts produce less IGF-I than fibroblasts from control; this finding can account for a reduced paracrine/autocrine action of IGF-I in these pts, in spite of a normal IGF-I plasma concentration. Addition of increasing concentrations of GH (0-100 ng/ml of medium) induced a dose-dependent increase of IGF-I in the conditioned medium with a maximum at 50 ng/ml of GH. Addition of EE (at 0-500 pg/ml of medium) also resulted in an increased production of IGF-I with a maximum already at 25 pg/ml of EE. The combination of increasing doses of GH with 50 pg/ml of EE was additive only in the fibroblasts from one pt.

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BONE MINERAL DENSITY IN GROWTH HORMONE-DEFICIENT CHILDREN. EFFECTS OF LONG-TERM GH THERAPY.

Bone mineral density, gr/cm2, (BMD) of the lumbar spine, L2-L4, was measured by dual energy X-ray absorptiometry (Lunar DPX) in 10 prepubertal GH-deficient children (8 boys and 2 girls, chronological age 7 to 12 years) and compared with that of 471 normal controls (256 boys, 215 girls, age range: 1-20 years). GH deficiency was established on the basis of: height < 3rd percentile, growth velocity < 5 cm/y, GH response < 10 ng/ml in two provocative tests, and bone age delayed of two or more years.

Before the start of GH therapy, BMD (mean +/- SD) was significantly reduced in GH-deficient children compared with normal age-matched controls (-1.64 +/- 1.08 n=10, p<0.001).

During GH therapy (0.6 - 0.7 IU Kg/BW/week, 14.3 +/- 2.45 months) all remained prepubertal, and a significant increase in growth velocity (8.08 +/- 1.56 cm/y, n= 10, p< 0.001), and in BMD (- 1.02 +/- 1.09, n= 10, p < 0.001) was observed in these patients.

In conclusion, BMD is reduced in GH-deficient children, and increases after long-term GH therapy. Our results underline the importance of GH in the maintenance of BMD in prepubertal children.

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PSYCHOSOCIAL STATUS OF GROWTH HORMONE DEFICIENT (GHD) PATIENTS IN ADULTHOOD.

The psychological and social status of adults previously treated in chilhood for short stature due to GHD has received little attention to date. These parameters were studied in a group of 28 adults with GHD: 16 with isolated GHD (treatment duration (td) : $\bar{X}$= 6.7 yr, final height (fh): -2.3 SD in 12 boys and -2.4 SD in 4 girls and chronologic age at evaluation (CAe): $\bar{X}$= 21.3 yr) and 12 with multiple pituitary GHD (td: $\bar{X}$= 9.9 yr, fh: $\bar{X}$= -2.0 in 9 boys and -2.3, 0.3, 0.5 in 3 girls and CAe: $\bar{X}$= 23.5 yr. All of them were idiopathic. A comparative study in the social aspects was performed in siblings. The study methods included: semistructured interview, special questionnaires and the following tests: Raven (intelligence), MMPI-Minnesota multiphasic personality inventory- (personality), STAI - State-treit (anxiety), Hamilton (depression) and CIMEC (local Spanish body image test). Patients showed different degrees of social maladjusment : social withdrawal, inhibition, parenteral dependency and depressive mood. The impact of short stature was never positive at school. In the cognitive area, academic achievement was low although intelligence quotients were normal. In contrast to their siblings the majority of patients failed to meet Spanish education standards. The unemployment rate was high. Self-esteem was generally low in both sexes. 60% had never experienced sexual intercourse and only 2 were married. Expectations of treatment were fulfilled in only 50% of cases. We conclude that GHD patients require psychological attention while undergoing GH treatment in chilhood.

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ESTRADIOL INHIBITION OF DNA-^{3}H-THYMIDINE INCORPORATION IN CULTURED HUMAN FETAL EPIPHYSEAL CHONDROCYTES .

Estradiol effects on DNA-^{3}H-thymidine incorporation by cultured human fetal epiphyseal chondrocytes incubated 96h in a serum-free medium were evaluated . Cells were in the presence of E_2 (0.001-100 nM) for the last 48h of incubation and ^{3}H-thymidine (5 µCi/ml) was added for the last 24h . E_2 (0.1 and 0.01 nM) significantly inhibits DNA-^{3}H-thymidine incorporation in cultured chondrocytes from 25-26-weeks-old male and female fetuses . In males (n=8) E_2 inhibition at 0.01 nM was 62.3 ± 21.4 (M ± SD) , (range 23.2-84.5) , controls=100 , (p= 0.0001-0.03) . In females (n = 5) E_2 inhibition at 0.01 nM was 55.6 ± 7.8 , (range 49.8-66.8) , controls = 100 , (p= 0.001-0.01) . No stastically significant differences in E_2 effects on cells from male and female fetuses were observed . In conclusion , E_2 exerts a biological effect on cultured human fetal epiphyseal chondrocytes . These results suggest that estrogens might be involved in growth regulation of human fetal epiphyseal cartilage

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hGH ASSAY IN URINE: PRELIMINARY RESULTS OF A FRENCH MULTI-CENTRIC EVALUATION. Coordinated by P. Georges[1], J. Liefooghe[2], L. Di Nicola[3], J.L.Chaussain[1]. 1: Hôpital St Vincent de Paul, Paris. 2: Faculté Libre de Médecine, Lille. 3:NOVO NORDISK PHARMACEUTIQUE, Boulogne, FRANCE.

Urines hGH was determined using E.I.A. commercial kit (NORDITEST) from NOVO NORDISK A/S. Inter-laboratory quality controls were performed in urines samples and standard calibrators: C.V. were between 18.5-29% at low concentrations (about 5 ng/l) and 10-15% for higher concentrations (about 20 ng/l). First morning urine samples were collected for 3 nights in 227 children (122 boys and 105 girls) mean age 9.0 (range 4 to 15 years) using plastic containers after addition of BSA solution (30% w/v). The following groups were studied: normal subjects (A), short stature with GH deficiency after pharmacological tests (B) and without GHD (C), nephrotic syndrome (D), diabetes mellitus (E), obesity (F), growth advance untreated (G) and somatostatin treated (H). The results expressed in u-hGH ng/mmol of creatinine, were:

Groupe	Number	Mean Age	u-hGH
A	97 (49 boys, 48 girls)	7y10m	1.63 (1.28 - 1.88)
B	20 (13 b, 7 g)	8y	2.24 (1.47 -3.01)
C	42 (24 b, 18 g)	8y 9m	2.07 (1.53 - 2.61)
D	5 (3 b, 2 g)	8y 8m	3.14
E	19 (9 b, 10 g)	11y	1.59 (0.8 - 2.38)
F	18 (10 b, 8 g)	10y	0.59 (0 - 1.40)
G	17 (12 b, 5 g)	10y6m	1.82 (1.0 - 2.65)
H	9 (2 b, 7 g)	13y	2.28 (1.14 - 3.43)

In conclusion, this study confirmed: (1) a decrease of u-hGH in obese patients, (2) in normal subjects no correlation with age between 4-15 years, (3) the pharmacological tests demonstrating both partial or total deficiencies in growth hormone secretion are not always ascertained by the hGH urine assay, (4) hGH urine assays are therefore of great interest in the screening of hGH total deficiency.

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FINAL HEIGHT (FH) AND SATISFACTION IN GH DEFICIENT ADULTS WHO WERE TREATED WITH GH IN CHILDHOOD. B.Rikken and J.M.Wit.

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The aim of this study was to investigate whether changes in therapeutic regimen in GH deficient (GHD) children over the years have resulted in improvement of FH and satisfaction of the patients. Until 1983 4 IU twice a week i.m. was given, until 1986 2 IU 4 times per week s.c., and since then 12-14 IU/m^2 per week in 6-7 injections, s.c.

A questionnaire was sent to all 661 GHD-patients treated since 1967, who were now older than 18 years and had discontinued GH therapy. To assess the validity of the *reported* FH we measured FH in 19 patients. The correlation between reported and measured FH was very high (r=0.995, p<0.001) with 65% of the patients reporting a FH within 1 cm of that of measured FH.

At present the results of 157 (M:F 112:45) patients have been analysed. Mean FH was 167.3 cm (-2.19 SDS) for males and 154.5 cm (-2.22 SDS) for females. There was no correlation between age at start of therapy and FH (r=0.04). For males there was a significant correlation between calendar year of start of GH and FH (r=+0.43, p<0.001). For each year that the treatment started later, FH was increased by 0.76 cm. For females there was no such correlation (r=0.02). Another factor which independently correlated with FH was, both for males and females, the coexistence of another pituitary hormone deficiency (MPHD). After correction for year of start of treatment, males with MPHD were 4.3 cm taller than males with isolated GHD. Females with MPHD were 5.4 cm taller than females with IGHD.

89.5% of the patients reported to be (very) satisfied with the result of the treatment. Satisfaction was significantly positively correlated with both FH and duration of treatment. In conclusion, the FH is unsatisfactory and in the same range as found in other countries. Over the years FH has ameliorated only in male patients. In contrast to the low average FH, most patients appeared satisfied with the result.