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SCREENING FOR COELIAC DISEASE BY DETERMINATION OF IGA GLIADIN ANTIBODIES IN CHILDREN WITH GROWTH-HORMONE DEFICIENCY AND IN CHILDREN OF SHORT STATURE. M. Colle, T. Lamireau, M. Appriou, J. Tribouley, Centre d'Endocrinologie Pédiatrique et Croissance, Hôpital des Enfants et Université de Bordeaux II - Bordeaux - France

Serum IgA gluten antibody levels (ELISA method) were measured in 83 children (53 boys and 30 girls - 11.1 ± 3.4 years of age) under growth hormone (GH) therapy (24.4 ± 4.1 months duration) for short stature (-2.87 ± 1.15 SD) due to GH deficiency (peak GH < 10 ng/ml at 2 provocative tests) as well as prospectively in 147 children (110 boys and 37 girls - 11.2 ± 3.3 years of age) without abdominal symtoms, normal body mass index (16.7 ± 2.3) and normal endocrinological evaluation referred to the outpatient clinic for short stature (-2.12 ± 0.83 SD). Elevated (≥ 30 units) gluten IgA antibody levels were detected in 8 children (2 GH-deficient and 6 non GH-deficient). Three of them (1 GH-D and 2 non GH-D) had probable coeliac disease based on villus atrophy at duodenal biopsy. Intestinal permeability assessed by excretion ratio of Lactulose and Mannitol was altered in these 3 patients. Three girls (1 GH-D and 2 non GH-D) with highly positive IGA antibodies had a normal duodenal biopsy. It is concluded that measurement of gluten antibodies, especially of the IgA type, should be included in the diagnostic evaluation of children with short stature as well as in the reevaluation of GH-treated children for GH deficiency. However, positive IgA gluten antibodies may be found in patients with normal intestinal mucosa.

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MT Tauber, P. Rochiccioli, JL. Rittié, C. Pienkowski, I. Oliver, P. Pigeon, C. Simonetta
Service d'Endocrinologie Infantile - CHU Purpan - Toulouse - France and Laboratoire Sandoz - Rueil Malmaison - France.

COMPARATIVE STUDY OF SOMATOSTATIN ANALOG VS. ESTROGEN IN TALL GIRLS (N = 20)

The treatment of constitutional tall stature in adolescent girls is based on high doses of Estrogen (Ethinyl Oestradiol - EE - 200 to 500 µg/day). Known vascular and metabolic risks led us to the use of other therapeutic means based on the reduction of GH secretion with Somatostatine Analog (SMS 201-995). This work consisted in comparing the results of a randomized protocol (SMS vs. EE) and the therapeutic efficiency of both medications.
20 girls aged 11 or more (n = 12, 1 ± 0.8 years) at the start of puberty (S2, P2 or S2, P3) whose prognostic height was more than 180 cm (Bayley Pinneau - BP) were treated upon request (and after randomization) either with SMS (100 µg twice a day SC) or with EE (200 µg daily + progesterone). A dosage of IGF1 (UI/ml) and a study of spontaneous GH secretion with the calculation of the 24h GH integrated concentration (24h IC ng/ml/min) were assessed before treatment and after 6 months of treatment. All twenty girls have now reached 6 months of treatment and will have been through 1 year of treatment by June 1993.
Mean parental height was 186.0 ± 5.3 cm for fathers and 173.3 ± for mothers. Mean height at the start of treatment was + 3.3 SDS and growth velocity (GV) during the year before treatment was 7.8 ± 1.5cm. There was no significant difference between the two groups in CA, BA, parental height, prior GV, pubertal development and height prognosis.
The results of treatment after 6 months are summed up in the table below:

	GV (-1yr) (cm/yr)	GV (+6m.) (cm/yr)	ΔBA (y) (0-6mth)	BP (day0)	BP (6mth)	IGF1 (day0)	IGF1 (6mth)	24h IC (day0)	24h IC (6mth)
SMS	7.7	2.7	1.4	181.3	170.3	334.5	258.2	4.6	3.7
EE	7.9	4.2	1.1	183.7	179.7	214.0	321.8	4.0	8.6

These preliminary results showed a greater efficiency of SMS than EE: Reduction of growth rate by 65% vs. 46%, significant decrease of IGF1 and 24h IC (whereas EE increased these two parameters). Side effects were observed by EE: 1 case of hypertension and 1 case of hypercholesterolemia required to discontinue treatment, with SMS a vesicular microlithiasis having subsided with desoxycholic acid and did not lead to therapeutic discontinuation.

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P. Rochiccioli, J. Battin, A.M. Bertrand, J.J. Bouquier, M. Bost, P. Chatelain, M. Colle, M. David, R. Freycon, J.M. Limal, G. Malpuech, R. Mariani, J.L. Nivelon, M. Pieron, G. Simonin, C. Sultan.
Service de Pédiatrie - CHU Purpan - Toulouse - France et Groupe d'Étude du Syndrome de Turner du Sud de la France.

STUDY OF FINAL HEIGHT IN TURNER SYNDROME (N = 216)

Understanding Turner syndrome spontaneous adult height is a prerequisite to an accurate assessment of the therapeutic efficiency of growth hormone treatment. The heights described in the literature reveal significant differences (136 to 147 cm). Our collaborative study pooled results from 16 pediatric endocrinology centers and obtained a great number of spontaneous adult heights (n = 216). The selective criteria were: chronological age (CA) > 18 years, bone age (BA) > 16 years, typical kariotype, no treatment with growth hormone nor anabolic steroids. Mean CA was 23.3 ± 5.6 years. Chromosomal anomalies were: monosomy X: 56.7%, mosaicism: 32.7%, structural aberration: 10.6%. Mean adult height in the whole group was: 141.5 ± 6.6 cm). There was no significant difference as to monosomy X (141.1 ± 6.4 cm for n = 121); mosaicism (141.5 ± 7.5 cm for n = 72); anomaly X (141.4 ± 5.0 cm for n = 23).
Mean parental height was 170.4 ± 7.1 cm (father) and 160.1 ± 6.2 cm (mother). Parental height and patients heights correlated significantly: more so with fathers' heights (r = 0.50) than with mothers' (r = 0.42). The correlation was still clearer with the target height (r = 0.55).
Individual patients heights varied greatly (ranged from 129 to 161 cm). The analysis heights in the 2 groups: > 146.6 cm (+ 1 SDS) n = 34 and < 134.8 cm (-1 SDS) n = 35 showed no difference in chromosomal anomaly distribution but revealed a very significant difference in parental height (158.3 ± 3.6 cm and 170.4 ± 4.9 cm respectively). These results showed: Turner syndrome adult heights were 4 SD below mean French heights, no difference in kariotype, a strong correlation with parental height and target height. Individual height differences can be explained by parental heights.

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P.J. Tapanainen, P. Bang, K. Wilson, H. Vreman and R.G Rosenfeld,
Department of Pediatrics, Stanford University, Stanford, CA 94305, USA

MATERNAL HYPOXIA AS A MODEL FOR INTRA-UTERINE GROWTH RETARDATION (IUGR): EFFECTS ON INSULIN-LIKE GROWTH FACTORS AND THEIR BINDING PROTEINS

Evidence suggests that IGFs and their binding proteins play a role in fetal growth but more knowledge of their regulation is essential. We examined the expression of IGFs and their binding proteins in experimental IUGR rat fetuses of hypoxic dams (13 % oxygen, days 14-21 of gestation). The mean body weight of the fetuses (day 21 of gestation, n=72) from the six hypoxic dams was 24 % lower ($p<0.0001$) than the mean weight of the fetuses of six control dams (n=82). Wet liver weights also demonstrated a 20 % decrease ($p< 0.0001$) compared to control fetuses. The mean concentrations of immunoreactive IGF-I were low in both groups but did not differ significantly. The mean concentrations of immunoreactive IGF- II were high, as reported earlier, but there was no statistical difference between the groups. As assessed by northern blot analysis there was an increase in IGFBP-1 mRNA expression in the livers of the IUGR fetuses compared to controls. IGFBP-2 mRNA expression was also increased in IUGR fetal liver. No difference was found in IGFBP- 4 mRNA. An increase in IGFBP-1, - 2 and - 4 could be seen in the serum of the growth retarded fetuses, compared to control fetuses, by Western ligand blotting. This finding was verified by immunoprecipitation with specific antibodies which showed similar increases in IGFBP-1 and IGFBP-2. Our results validate the use of maternal hypoxia as an experimental model of IUGR and indicate that increased IGFBP-1 and -2 expression may be of importance in the etiology of fetal growth retardation caused by maternal hypoxia.

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B.J. Otten, C. Rongen-Westerlaken, B.A.C.M. v.d. Velden.
Department of Pediatrics, Radboud University Hospital, Nijmegen, the Netherlands.

TREATMENT OF PATIENTS WITH MIXED GONADAL DYSGENESIS (KARYOTYPE XO/XY) WITH BIOSYNTHETIC GROWTH HORMONE 24 U/m^2/WEEK RESULTS IN INCREASED GROWTH VELOCITY: TWO YEAR RESULTS.

Five patients with mixed gonadal dysgenesis (karyotype XO/XY) were treated with biosynthetic growth hormone (GH) for two years. Three patients (1, 2 and 3) presented with ambiguous genitalia at birth and after treatment were reared as girls. The other two (4 and 5) were reared as males. Standard GH-stimulationtests, as well as 24 h. GH profiles performed prior to treatment were in the normal range. GH dosis used was 24 U/m^2/week S.C. given in 6 daily doses.
Results

Pat. no.	Age at start yr	Bone Age start yr	Growth velocity cm/yr Bef.	1st. yr	2nd. yr	bone age (yr) 0-2 yr	prediction cm
1	10.8	9.0	5.1	7.9	5.7	1.5	+ 7.5
2	13.2	10.0	2.9	6.4	5.9	1.0	+ 5.8
3	13.5	10.0	2.9	6.1	6.8	1.5	+ 5.1
4	12.2	12.0	3.5	7.9	7.2	1.0	+10.3
5	13.1	12.5	3.9	9.5	8.5	1.0*	+ 2.0*

* 1 year follow-up.

It is concluded that in XO/XY karyotype, treatment with GH in a dose of 24 u/m^2/ week results in a significant increase in growth velocity in the first 2 years of treatment and in an increase in height prediction.

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ANALYSIS OF THE RADIAL METAPHYSEAL BAND, HEIGHT VELOCITY AND IGF-I LEVELS IN ISOLATED GROWTH HORMONE DEFICIENT PATIENTS. A. Tar, I. Szécsényi-Nagy and F. Péter, Buda Children's Hospital, Budapest, Hungary

30 prepubertal (26 boys, 4 girls) isolated growth hormone (GH) deficient children were studied before and after one year treatment (0,5 U/kg/week Genotropin, Norditropin and Saizen). 12 of them (11 boys, 1 girl) were analysed after two years on GH therapy too.
Measurement of metaphyseal band (MB) was completed by Protomix LTD medical image processing and archiving microprosessor based system. After the first year of treatment the average ($\bar{x}\pm SD$) MB grew from $0,92\pm0,46$ to $1,71\pm0,63$ mm; $\bar{x}IGF\text{-}I: 63,4\pm57,7$ to $215,5\pm208,5$ ng/ml; $\bar{x}HV: 2,0\pm1,4$ to $8,5\pm4,0$ cm. In the second year the average MB diminished: $1,43\pm0,46$ mm; $\bar{x}IGF\text{-}I$ changed to $214,1\pm225,0$ ng/ml; $\bar{x}HV: 10,2\pm3,9$ to $7,2\pm2,6$ cm ($p<0,001$).
Comparing the change in HV, MB and plasma IGF-I levels, correlation was found only in the second year of treatment between BM and IGF-I levels.
Conclusions: 1. The MB, the HV, plasma IGF-I significantly grew during the first year of treatment.
2. In the change of MB the role of IGF-I could be suspected: a., both parameters significantly grew during the first year; b., in the second year on GH treatment both the HV and MB diminished, simultaneously with the change in IGF-I levels.