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PATTERNS OF GROWTH AND DEVELOPMENT IN 26 CHILDREN OPERATED FOR ADRENOCORTICAL CARCINOMA (ACC) AND DISEASE-FREE FOR MORE THAN ONE YEAR. Schmit-Lobe, M.C. De Lacerda, L., Ribeiro, R., Kohara. S.K. Sandrini, R. Division of Endocrinology, Department of Pediatrics, Federal University of Paraná, Curitiba, Brasil.

Chronic exposure to sex steroids during childhood accelerates skeletal maturation and may compromise final height. The growth of 26 children (18 girls, 8 boys) disease-free of ACC for more than 1 yr were reviewed. The initial clinical signs appeared at 2.9 ± 2.8 yr and the diagnosis was made at 3.6 ± 2.8 yr. Time of follow-up after surgery was 6.2 ± 3.5 yr (range 1.5 - 13.0). 50% had adrenogenital syndrome (AS), 38% mixed syndrome (MS: Cushing's plus AS), 8% no endocrine symptoms and 4% Cushing syndrome. At the time of diagnosis the mean H-SDS was higher than target height-SDS (TH-SDS; $p < 0.0001$). H-SDS was not different between AS and MS groups ($p > 0.1$). Bone age (BA; 6.2 ±3.6) was greater than height age (HA; 4.2 ± 2.7) and chronological age (CA; 3.8 ± 2.9) ($p < 0.05$), whereas HA and CA were not different. BA advanced more than CA in the 1st year following tumor removal; in the 2nd year and thereafter we observed catch-down growth that was more intense in BA than in H-SDS. Only one patient of the series, with no BA catch-down, developed true precocious puberty. Initial predicted adult height (PAH; Bayley & Pinneau) of 10 patients was lower than target height (TH; $p < 0.01$); however, in the last evaluation (16 pts) PAH and TH were not different ($p > 0.1$). In conclusion: a) children exposed to androgen with/without glucocorticoid for a limited period of time usually increase BA more than H-SDS; b) after tumor excision both BA and H-SDS exhibit catch-down growth that is more pronounced for BA; c) despite the initial advancement of BA it appears that the final height is not compromised.

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DIFFERENT HORMONAL PATTERNS IN PREPUBERTAL HYPERTRICHOSIS.

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Prepubertal idiopathic hypertrichosis (PIH) is characterized by excessive growth of vellus hair. In a previous study of 17 girls with PPH, most of them showed elevated levels of androstenediol-glucuronide in serum, suggesting increased peripheral 5α reductase activity. In order to complete this study and to clarify these hormonal alterations, twenty-nine girls with PIH, ages 0.8 to 8.2 years and nine age- matched girls were studied. Dehydroepiandrosterone sulphate (DHEAS), testosterone (T), androstenediol glucuronide (Diol-G) were determined by RIA, and SHBG by DHT binding. The free androgen index (FAI) was calculated. We found three groups of patients with different androgen patterns: A) 10 girls had a normal pattern, B) 9 girls had elevated FAI and C) 7 girls had elevated Diol-G. Three girls showed elevated FAI and Diol-G and were analized separately.

RESULTS:	Controls	Group A	Group B	Group C
T(nMOL/L):	0.67± 0.26	0.56± 0.21	0.89± 0.32	0.68± 0.23
SHBG(nMOL/L):	71.16±13.41	77.54±28.90	57.54±15.20	97.74±26.70
FAI:	0.90± 0.45	0.71± 0.23	1.56± 0.31*	0.75± 0.30
A(nMOL/L):	1.61± 0.93	1.72± 0.85	2.37± 1.11	2.23± 1.11
DHEAS(uMOL/L):	0.57± 0.34	0.38± 0.19	0.65± 0.65	0.39± 0.33
Diol-G(nMOL/L):	1.22± 0.48	1.34± 0.60	1.33± 0.61	3.22± 1.38**

* $p < 0.01$ B vs Controls, A & B. ** $p < 0.01$ C vs Controls, A & B.

65% of the 29 girls with PIH showed pathologic hormonal patterns; 31% showed elevated FAI; 24% elevated Diol-G and 10% elevated FAI and Diol-G. 35% showed normal androgens, Diol-G and FAI. This study demonstrates that most of the girls with PIH exhibit pathologic hormonal patterns, although a small group of patients did not show any alteration in the parameters studied.

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EFFECT OF CHRONIC SOMATOSTATIN SUPPPESSION DURING TREATMENT WITH GH RELEASING FACTOR (GHRH). Mericq, V., Cassorla, F., García, H., Avila, A., Boric, M.A., Merriam, G. IDIMI, University of Chile, Santiago, Chile and DEB, NICHD, NIH, Bethesda, Maryland, U.S.A. Supported by Fondecyt 91-1020.

To evaluate the effect of chronic suppression of somatostatin during treatment with GHRH, we studied in a double-blind and cross-over study 13 prepubertal children with growth hormone deficiency (7F, 6M) ages 3 11/12 to 16 8/12 years. Each patient was studied prior to, and 12 and 24 months after starting treatment to determine plasma GH concentrations every 20 minutes during 24 hours, IGF-1 and IGFBP-3. Height was measured every 6 months. Treatment consisted of GHRH 20 ug/Kg/day sc + atenolol 1 mg/Kg/day or placebo during 12 months. Patients crossed over to the alternative treatment during the following 12 months. Spontaneous GH concentrations were analized by the Pulsar method. Results are shown in the table.

	Growth vel(cm/yr)			IGF-1(ng/ml)			IGFBP-3(mg/L)			Mean GH(ng/ml)		
	0m	12m	24m	0m	12m	24m	0m	12m	24m	0m	12m	24m
GRF+Ate-nolol	2.5±0.6	8.8*± 1.2	3.5± 1.3	91± 89	87± 64	67± 49	2.5± 1.2	3.8± 1.7	3.4± 2.1	1.3± 0.7	2.0± 1.2	1.9± 1.3
GRF+Pla-cebo		5.1± 1.4	4.4± 1.3		84± 63	63± 48		4.7± 2.6	3.8± 1.5		1.4± 0.3	2.4± 1.4

(* $p < 0.05$ compared to placebo)

Conclusions: 1. -Chronic blockade of somatostatin secretion enhances growth velocity during the first year of GHRH treatment. 2. -There is a tendency for the mean GH concentration to be greater in the group treated with atenolol, but this does not reach statistical significance. 3. -There is no significant difference in plasma IGF-1 and IGFBP-3 between the groups treated with GHRH plus atenolol or GHRH plus placebo.

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IGF-1 AND IGFBP-3 REMAIN HIGH AFTER TREATMENT-INDUCED PUBERTAL ARREST IN GIRLS WITH CENTRAL PRECOCIOUS PUBERTY (CPP). Kauschansky, A., Karasik, A., Pariente, C., Kanety, H. Ped. Endocr. Clinic, Hasharon Hosp., Dept. Ped. C. CMCI, Petah Tiqva, and Inst. Endocrinol. Sheba Med. Ctr., Tel-Hashomer, Israel. Tel Aviv Univ. Medical School, Israel.

Insulin like growth factor-1 (IGF-1) increases during normal adolescence and in CPP secondary to the rise in sex steroids and GH. Treatment of CPP using GnRH analog suppresses GH as well as gonadotropins. We examined IGF-1 and its major binding protein-IGFBP-3 in sera of ten girls diagnosed with CPP, before and during the first 3 months of GnRH analog therapy. Serum IGF-1 was increased in patients with CPP as compared with controls (48.8 + 6.5 vs 23.1 + 4.9 nmol/L, $p < 0.01$). GnRH analog therapy caused serum E_2 levels to return to prepubertal levels in all 10 patients, whereas serum IGF-1 levels decreased minimally after one (43.2 ± 5.6 nmol/L), two (42.3 ± 6.4 nmol/L), and three (44.1 ± 7.2 nmol/L) months of therapy. Serum IGFBP-3 concentrations measured using IRMA were also higher in CPP compared with controls (4.7 ± 0.37 vs 3.7 ± 0.42 mg/L $p < 0.01$). These differences were also evident when all IGF binding proteins were measured by Western ligand blotting. GnRHa therapy caused a small and insignificant decrease in serum IGFBP-3 levels after one (4.57 ± 0.33 mg/L), two (4.48 ± 0.4 mg/L) and three (4.42 ± 0.3 mg/L) months of therapy. This lack of suppression of both IGF-1 and IGFBP-3 despite therapy which halts pubertal progression and reverses GH secretion underscores the complex regulation of IGF-1 and its binding proteins during puberty.

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CHANGES IN BONE MINERAL DENSITY, GROWTH VELOCITY AND RENAL FUNCTION IN UREMIC PREPUBERTAL CHILDREN TREATED WITH GROWTH HORMONE.

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Thirteen prepubertal uremic children (mean glomerular filtration rate of <20.8 ml/min/1.73 m^2) and short stature (H-SDS -3.5) were treated with growth hormone (Genotropin; 1 IU/Kg/week subcutaneously daily) for 12 months. Growth velocity increased significantly from 4.3 ± 2.1 to 9.6 ± 3.2 and 9.1 ± 2.0 cm/year at 6 and 12 months of treatment without acceleration of bone age and with a significant improvement in H-SDS (from -3.5 ± 1.0 to -3.1 ± 1.1 and -2.6 ± 1.3 respectively at 6 and 12 months). Renal function of the patients as a group did not deteriorate. Total bone mineral content, as well as cortical and trabecular bone mineral density was significantly decreased in patients before treatment with growth hormone; these values increased significantly with treatment reaching levels similar to those of a control group of healthy children. Total bone mineral content increased from 531.2 ± 88.5 to 698.5 ± 81.8 g, while cortical and trabecular bone mineral density increased from 0.591 ± 0.041 and 0.429 ± 0.045 g/cm^2 to 0.690 ± 0.069 and 0.672 ± 0.058 g/cm^2, respectively after 12 months of growth hormone therapy. Trabecular bone mineral density increased significantly in our patients compared to a control group of uremic children followed without GH therapy. These studies demonstrate that prepubertal uremic children have a diminished bone mass which increases reaching normal values following treatment with recombinant human growth hormone; their growth velocity also increases significantly, without apparent deterioration of renal function.

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INFLUENCE OF PHYSICAL ACTIVITY ON SKELETAL MINERALIZATION.

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The achievement of an optimal peak bone mass in the second decade of life is the best protection against fractures later in life. Physical exercise contributes to maximal skeletal mineralization in adults. However in adolescents, physical activity (PA) can reduce skeletal mineralization in some sports, while it can improve it in others. The purpose of the present study was to analyze the influence of PA upon skeletal mineralization. This was evaluated by determining bone mineral density (BMD) in total body, lumbar spine and femoral neck, measured by double-photon isotopic absorptiometry (Norland). 144 school children of both sexes, between the ages of 7 and 14 years, with different degrees of PA were recruited. Results were expressed as the mean ± SEM and the level of significance was evaluated by the Student t and F test. With increased physical activity, higher BMD mean values in the femoral neck and the lumbar spine were observed in both sexes. If physical activity was increased, BMD was 110% of the normal standard for pubertal and 108% for prepubertal children. In pubertal school children with decreased PA, BMD was below the normal standard. These results suggest that PA increases skeletal mineralization in the lumbar spine and femoral neck, particularly during puberty.