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IGF-1 AND IGFBP-3 LEVELS IN NORMAL CHILDREN AND CHILDREN WITH DISORDERS OF GROWTH. Silva, E., Pelegrinelli, A.C., Borges, M.F., Montovani, E., Pradal, M., Nicolau, W., Arnhold, I.J.P., Mendonca, B.B. Department of Endocrinology, HCFMUSP, Triângulo Mineiro, Medical School, Brasil.

Recent development of a specific radioimmunoassay for IGFBP-3 permits its measurement in disorders of the GH-IGF-1 axis. To establish normal IGF-1 and IGFBP-3 values in our population, serum was drawn from 86 normal children of both sexes and different stages of puberty and compared to 7 patients with short stature with normal GH tests, 10 with GH deficiency (confirmed by 2 stimulation tests) and 3 with precocious puberty. IGFBP-3 assay was performed by CRIESP - Central de Radioimmunoassay de Sao Paulo with a commercial kit from DSL according to the method of Miles et al. There is no cross-reactivity with other binding proteins (IGFBP-1,2 and 4). The sensitivity was 0.5 mg/L and intra - and interassay coefficients of variation were below 4.0%. IGF-1 was assayed at the Radioimmunoassay Laboratory of the Hospital das Clinicas after ethanol extraction using a kit from Nichols.

TANNER	SEX (N)	AGE GROUP (years)	IGF-1 ng/mL	IGFBP-3 mg/L	DHEAS ng/mL	T(M)-E2(F) ng/dL-pg/m
I	M (27)	1.7-12.0	112± 57	2.5±0.5	84±112	19±7
	F (13)	1.2-11.9	180± 94	2.4±0.6	125±133.5	12±5
II + III	M (21)	9.8-16.5	230± 86	3.2±0.6	450±524	154±142
	F (09)	9.0-13.3	294±109	3.4±0.6	309±284	22±19
IV + V	M (07)	13.0-17.9	360±93	3.7±0.7	297±240	478±99
	F (09)	11.9-17.5	366±175	3.0±0.7	473±299	45±36

Results among normal children were compared by unpaired Student t-test. There was no statistical difference between IGFBP-3 and DHEA-S in males and females, whereas IGF-1 levels in Tanner pubertal stages I to III were significantly higher in females. IGFBP-3 was normal in the 7 patients with short stature, low in 60% of patients with GH deficiency, 25% of which had low IGF-1, compared to controls. The 3 patients with precocious puberty had normal IGFBP-3 levels for pubertal stage.

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SERUM IGF-1 AND IGF-BINDING PROTEIN-3 LEVELS BEFORE AND AFTER RENAL TRANSPLANTATION (TX).

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Failure of growth is frequent in patients (P) with end stage renal disease (ESRD) and after renal TX. We studied serum IGF-1 and IGF-binding protein-3 (IGFBP-3) levels (RIA) in 18 ESRD P on dialysis 8.0-29.5 years old (x:18.7), and in 19 TX P 4.7-21.8 years old (x:12.9). ESRD P had lower mean IGF-1 levels (x±sd:0.66±0.25 U/ml) than TX P (1.77±0.89 U/ml, $p < 0.001$). In contrast, mean IGFBP-3 was higher in ESRD P (8.0±2.43 mg/L) than in TX P (5.78±1.21 mg/L, $p < 0.001$). Mean IGFBP-3 levels in both groups of P (6.86±2.19 mg/L) was higher than in controls (n=38) (4.53±1.47 mg/L, $p < 0.001$). When P were divided in Tanner I (n= ESRD:6 & TX:11) and Tanner IV-V stages (n= ESRD:11 & TX:8) IGF-1 and IGFBP-3 levels were:

	IGF-1 (U/ml)			IGFBP-3 (mg/L)		
	ESRD	TX	p <	ESRD	TX	p <
Tanner I	0.6±0.3	1.4±0.7	0.01	8.6±3.8	5.1±0.9	0.01
Tanner IV-V	0.7±0.2	2.3±0.9	0.001	7.6±1.5	6.6±1.0	NS
p <	NS	0.05		NS	0.01	

IGF-1 levels correlated with height SDS for chronological age in ESRD (r:0.63) and in TX P (r:0.67). In TX P, there was a significant correlation between IGFBP-3 and IGF-1 levels (r:0.53), and between IGFBP-3 and Tanner stage (r:0.56). We conclude that increased levels of IGFBP-3 may be implicated in IGF inhibition. The physiologic elevation of IGF-1 levels during puberty was observed in TX P but not in ESRD P.

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HIGH PLASMA LEVELS OF IGF-1 AND IGF-II IN SMALL FOR GESTATIONAL AGE (SGA) VERSUS APPROPRIATE FOR GESTATIONAL AGE (AGA) INFANTS IN THE THIRD DAY OF LIFE. ¿COMPENSATORY POST-NATAL GROWTH?. García, H., Henríquez, C., Beas, F., Ugarte, F., Iñiguez, G. IDIMI, University of Chile. Santiago, Chile.

We studied the hormonal levels of newborns, during the third day of life in 47 SGA infants with a mean weight of 2.29 kgs. and mean length of 45.5 cms, and in 40 controls AGA infants with a mean weight of 3.37 kgs. and mean length of 49.1 cms.

There were no significant differences between SGA and AGA newborns in the serum concentrations of Insulin: 45±5.4 vs 40±4.1 uUI/ml; Prolactin: 184±38 vs 162.8±51 ng/ml; T4: 13.1±3 vs 15.3±2.5 ug/dl; T3: 143±47 vs 151±42 ng/dl; Testosterone: 1.6±1.5 vs 1.2±1.1 ng/ml and Estradiol: 495±±18.1 vs 501±23.4 pg/ml respectively, but there was a significant difference in IGF-I and IGF-II levels.

	IGF-I ng/ml	IGF-II ng/ml
AGA	9.1±14.4	27.2±13.7
SGA	22.4±25.8 ($p < 0.001$)	38.9±35.0 ($p < 0.05$)

It is known that IGF-I and to a lesser extent IGF-II in cord blood are correlated with newborn size. The higher plasma levels observed on the third day of life in SGA infants may signal the beginning of compensatory mechanisms of post natal growth in these children.

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CLINICAL AND MOLECULAR STUDIES OF 21 BRAZILIAN FAMILIES WITH CLASSIC CONGENITAL ADRENAL HYPERPLASIA (CAH) DUE TO 21-HYDROXYLASE DEFICIENCY. Guerra Jr. G., Mello,M.P., Farah,S.B., Araujo, M., Baptista,M.T.M., Marini,S.H.V.L. Division of Pediatric Endocrinology. CEBEMEG - UNICAMP, Campinas -Sao Paulo - Brasil.

The genetic organization of the 21-OHase complex (P450c21) in CAH is well characterized, but the findings reported in the literature vary depending on the population studied. This investigation was carried out to determine the genetic alterations of the P450c21 complex in Brazilian families. During 18 months, we studied 21 families with 27 affected individuals with classic 21-OHase deficiency. Blood samples of all family members were tested for hybridization on conventional Southern blot with Taq I digests of DNA, with gene probes for P450c21 and C4. Among the 27 affected individuals (9M:18F, with positive family history in 11/21, and consanguinity in 4/21), 9 had the simple virilizing and 18 the salt-wasting form. The most frequent alteration was a point mutation of the 21B gene with a normal 21A gene (64.8%). These results are similar to those published in the literature. However, the presence of 5.5% deletions and 16.8% conversions of the 21B gene in our population, indicate the need for further studies to confirm these findings.

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STUDY OF THE CYP21 GENE IN AN ARGENTINIAN POPULATION OF PATIENTS (P). WITH 21-HYDROXYLASE ENZYME DEFICIENCY (CAH).

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Seventy five percent of lesions of the CYP21B gene are point mutations (PM) and 25% are gene deletions or macroconversions (D/C). In a previous study, using PCR followed by restriction enzyme or SSCP analysis, we identified the genetic lesion in 50 % of the alleles in the salt/losing (SL) form, but in none of the alleles in the simple virilizing (SV) form. In this study we have added a dot-blot technique using specific oligonucleotides in order to evaluate the most frequently described mutations in American and European populations. A total of 18 affected families were studied,(12 SL and 6 SV). Four different regions of the CYP21B gene were amplified by PCR. In SL, D/C was studied by PCR, PM of codon 318 (C -> T) and of exon 3, -8bp by PCR associated with restriction endonuclease (Pst 1 and Alu 1 respectively), PM of codon 234-238 (T,T,T -> A,A,A) codon 356 intron 2 (A -> G) and codon 172 (T -> A) by PCR associated to hybridization with specific oligonucleotides. The last 2 MP were also looked for in SV. In SL, mutant CYP21B genes were detected for 71% of alleles (D/C:25%, Intron 2:20.8%, codon 318:16.7%, -8bp:8.33%, codon 234-238:0%, and codon 356:0%), and in SV in 30% (codon 172:30%, intron 2, 0%). The fact that no PM was detected in intron 2 of SV (vs 30% in other populations) suggests that other PM are present in our population.

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EVALUATION OF BONE MASS IN MALE PSEUDOHERMAPHRODITES (MPH) RAISED AS FEMALES. Costa,E.M.F., Arnhold,I.J.P., Cassina,C., Ribeiro,AP., Batista,M.C., Bloise,W., Leite,M.O.R., Borelli,A., Mendonca,B.B. Gonads and Intersex Unit, Division of Endocrinology and Department of Radiology, University of Sao Paulo School of Medicine, Sao Paulo, Brazil.

Evaluation of bone mass in castrated MPH has not yet been reported in the literature. Our goal was to study bone mass after the onset of puberty in a group of 19 MPH raised as females, by measuring bone mineral density expressed as Z score with a Hologic QDR-1000 densitometer. Patients were divided into 2 groups: Group I - 7 patients with complete (4 cases) or partial (3 cases) androgen insensitivity, who had been castrated after puberty; Group II - 12 patients with MPH due to various causes, who had been castrated before puberty, and started on estrogens either before 12 years (Group II A) or after 16 years (Group II B) of age. Results are expressed as mean ± standard deviation.

GROUP	n	Z score
I	7	-1.54±0.78
II A	5	-1.00±0.48
II B	7	-2.45±1.01

All patients in Group I (except for 2 cases with Z score of -2.16) and also in Group IIA had a bone mass within the normal limits. In Group IIB, all subjects had a bone mass below -2 standard deviations, (except for one case with a Z score of -0.49). We conclude that most patients with androgen insensitivity who were castrated after puberty, and all subjects with various causes of male pseudohermaphroditism who were castrated in childhood and started on estrogen before the age of 12, had normal bone mass. The presence of endogenous or exogenous estrogen at the time of puberty appears to be important for the maintenance of normal bone mass.