

MACROPROLACTINOMA IN ADOLESCENTS: THREE CASES TREATED WITH BROMOCRIPTINE. Reyes, M.C., Campusano, C., Cattani, A. Departments of Pediatrics and Endocrinology, Catholic University, Santiago, Chile.
 Macroprolactinomas (M) seem to be infrequent in individuals below 18 years of age. In adults bromocriptine (BC) therapy has been successful, but few data have been reported in adolescents. We report the clinical course and hormonal response to BC in three adolescents with M. (Case 1) A 14-year-old girl with secondary amenorrhea, galactorrhea and headache. Height 155 cm; weight 25 kg; Tanner stage IV. PRL 17.5 ng/ml; TSH 2.3 µU/ml; normal; FT₄ 0.5-1.1 ng/dl; LH 1.2 U/ml; FSH 14.9 mIU/ml (8-20); CT scan: intrasellar mass with sphenoidal sinus invasion, 20 mm in diameter; Goldmann's perimetry (GP): normal. She received 7.5 mg of BC per day, and after 4 months PRL and menses were normal. After two years of follow-up, she is normoprolactinemic with 5 mg daily of BC and complete resolution of tumor (Case 2) A 17.6-year-old girl with primary amenorrhea, headache and visual loss. Height 150 cm; Tanner stage III. PRL 799 ng/ml; TSH 2.3 µU/ml; FT₄ 9.8 ng/dl; FSH 3.9 mIU/ml; LH 4.5 mIU/ml; E₂ 49 pg/ml; CT: solid-cystic supra/intrasellar mass, 13 mm in diameter; GP: bilateral temporal field deficit. One year after BC 22.5 mg daily, PRL decreased to 191 ng/ml, but the amenorrhea has persisted. She experienced tumor shrinkage (60%) and normalization of visual fields. (Case 3) An 18-year-old boy with delay in growth and puberty. Height 163 cm; excess abdominal fat and Tanner stage III. PRL 1518 ng/ml; GH stimulation test with Clonidine: maximal response: 0.8 ng/ml; bone age (chronological age-15.2/18); CT: solid-cystic supra/intrasellar mass, 19 mm in diameter; GP: normal. After 5 months of treatment with BC, PRL and GH were normal, and there was complete resolution of the tumor. After 1.5 years he presented catch-up growth, progression of puberty and he remains normoprolactinemic with 7.5 mg daily of BC. (Conclusions) In our experience, BC is effective in the treatment of M, even with visual field deficits or hypopituitarism. Tumor shrinkage improves surgical approach, even if normoprolactinemia is not achieved. We observed dissociation between tumor size reduction and suppression of PRL, as described in the literature. In our patients BC was well tolerated.

IMPROVED ASSAY SENSITIVITY FOR SERUM LH AND FSH IN NORMAL CHILDREN AND ADOLESCENTS. Ropelato M.F., Escobar M.F., Gottlieb S., Bergada C. Division of Endocrinology, Ricardo Gutiérrez Children's Hospital, Buenos Aires, Argentina.
 The onset of puberty is associated with an increase in LH and FSH secretion. A 2- to 6- fold increase in gonadotropin levels has been shown using RIA, with monoclonal antibody assays, greater changes in LH secretion have been observed. In order to document changes in gonadotropin secretion during childhood and puberty, serum basal levels of LH and FSH by IRMA (MDP:0.02 IU/L) and by RIA (MDP:0.10 IU/L) were measured in normal children and adolescents (28F, 29M). Serum LH and FSH basal levels (xSD) in relationship to chronological age (years), sex and pubertal development (P) are shown in the table.

	IRMA-RIA LH IU/L (IRP 68/40)	IRMA/RIA FSH IU/L (IRP 69/104)
Girls (3)	0.1 (1)	0.1 (1)
Boys (4)	0.1 (1)	0.1 (1)
28F	0.1 ± 0.1 (1)	0.1 ± 0.1 (1)
29M	0.1 ± 0.1 (1)	0.1 ± 0.1 (1)

COMPARISON OF GROWTH HORMONE (GH) LEVELS MEASURED BY IMMUNORADIOMETRIC (IRMA) AND IMMUNOFUORIMETRIC ASSAYS (IFMA) IN CHILDREN OF SHORT STATURE. Garul, S., Lemos, M.M., Cassina, C., Osorio, G.F., Oliveira, S.R., Silva, F., Batista, M.C., Nicolai, W., Arnold, J.J.P., Mendonca, B.B. Department of Endocrinology and Laboratory of Radioimmunoassay - HCFMUSP, Sao Paulo, Brazil.
 Traditionally, the diagnosis of GH deficiency is based on maximal GH values after two stimulation tests under 7 ng/ml measured through IRMA. There are now more sensitive methods to measure GH, such as IFMA. In this study we compared the GH response measured by IRMA and IFMA in a group of 9 children (3M; 6F) with short stature (SD for stature between -1.2 and -3.7) who were considered normal through two pharmacological tests for GH measured by IRMA. We also assessed by IFMA the GH responses to stimulation tests in patients with proven GH deficiency (transection of pituitary stalk associated with hypoplastic pituitary and ectopic neurohypophysis or multiple hypothalamic-pituitary deficiencies) or strong clinical evidence (SD for height < -3.06) and low values of IGF-1. The IRMA and IFMA detection limit was 0.25 ng/ml and 0.1 ng/ml respectively.

SEX	AGE (yr)	HEIGHT (cm)	SDS	TEST	Bas IRMA Peak (ng/ml)	Bas IFMA Peak (ng/ml)
F	4.0	93.7	-2.6	CLO	0.3	0.24
F	4.0	102.3	-3.4	CLO	2.2	1.42
F	6.0	109.7	-1.7	ITT	0.47	0.28
F	6.0	122.0	-1.6	ITT	0.34	0.25
F	8.0	116.0	-2.8	CLO	0.24	0.1
F	10.0	120.0	-2.6	ITT	0.1	0.06
F	10.0	120.0	-2.6	ITT	0.1	0.06
M	14.0	147.7	-1.7	CLO	0.3	0.1

RAT GH RECEPTOR/GH-BINDING PROTEIN mRNAs WITH DIVERGENT 5'-UNTRANSLATED REGIONS ARE EXPRESSED IN A TISSUE- AND TRANSCRIPT-SPECIFIC MANNER. Domene, H.M., LeRoith, D., Roberts, Jr. C.T., Cassorla, F. Developmental Endocrinology Branch, NIDDK, and Diabetes Branch, NIDDK, NIH, Bethesda, Maryland, U.S.A.
 In the rat, the growth hormone receptor (GH-R) gene generates two transcripts, one that encodes for the GH-R, and a shorter one that encodes for the GH-binding protein (GH-BP). The mRNAs encoding for these transcripts present a high degree of heterogeneity in the 5'-untranslated regions (5'-UTR). It seems likely that some of the exons encoding 5'-UTR variants may be flanked by distinct promoter regions. The activity of different promoters could result in the tissue-specific expression of these variants. To assess this possibility, we used PCR amplification to characterize the 5'-UTR variants of rat GH-R mRNA, and by using 5'-UTR-specific probes, we determined their pattern of expression in several tissues in the rat. In addition to two previously described variants (V1 and V2), three new 5'-UTR variants were identified, extending 56 nt. (V3), 135 nt. (V4), and 209 nt. (V5) upstream of the ATG translation initiation codon. The study of tissue distribution revealed that variant V1 and V5 exhibited a pattern of expression resembling that of exon 2. Variant V2 was exclusively expressed in liver. Variant V4, although present in liver, was more abundant in extrahepatic tissues, and predominantly found in GH-R transcripts. Variant V3 was expressed at low levels. These findings support the concept that different 5'-UTR variants are the result of different promoters acting in a tissue-specific manner. The association of specific 5'-UTR variants with either GH-R or GH-BP mRNA transcripts raises the possibility that the alternatively splicing process that generates GH-BP in the rat might be controlled by the 5'-flanking region driving specific leader exons.

REGULATION OF INSULIN DEGRADING ENZYME. Pérez, A., Cambercos, M.C., Zuazquita, A., Cresto, J. C. FEDIE, Ricardo Gutiérrez Children's Hospital, Buenos Aires, Argentina.
 The main enzyme that triggers and controls insulin degradation is the insulin degrading enzyme (IDE). Many mechanisms have been postulated for IDE regulation but none has been conclusively proven. Highly purified rat liver cytosolic IDE was prepared by: 1) precipitation with ammonium sulphate, 2) DEAE-Sephadex with NaCl gradient, 3) pentylagarose with ammonium sulphate gradient, 4) chromatofocussing in FBE94. Insulin degradation by IDE was inhibited with ATP (0.05-4 mM) and GTP (1-8 mM) in dose-dependent fashion. AlF₃ (0.05-40 mM) had the same effect in the presence of Mg²⁺, but not NaF. Mg²⁺ suppression does not change AlF₃ inhibition. G-protein participation in this inhibition was excluded since these are activated with AlF₃, only if Mg²⁺ is present.
 We conclude: 1) ATP inhibits IDE at physiological concentrations, while GTP acts as a phosphate donor at the concentrations used; 2) the G-protein participation in IDE inhibition could not be demonstrated in our system.

EPIDEMIOLOGY AND IMMUNOGENETICS OF INSULIN-DEPENDENT DIABETES MELLITUS IN VENEZUELAN CHILDREN. Gunczler, P., Lanes, R., Leyrisse, Z., Balducci, P., Esparza, B., Sales, R., Arnaiz-Villena, A. Clinicas Hospital Caracas. Scientific Research and Hygiene Institutes, Caracas, Venezuela and 12 of Octubre Hospital, Spain.
 We evaluated 91 newly diagnosed IDDM children mean age 7.8 ± 4.5 yrs; 56.7% had had an upper respiratory infection prior to diagnosis and 12.7% had had either mumps or varicella. Peak incidence of disease was found in February and March and August to October. Eighty seven percent had HLA-DR3 and/or DR4 vs 37% of the Venezuelan general population; 81.6% were HLA-DQW2 and/or HLA-DQW8. Studies of oligonucleotide hybridization showed the presence of arginine in position 52 of the DQ alpha chain and absence of aspartic acid in position 57 of the DQ beta chain, with an increased prevalence of DR2 and especially with DQB1 0602 which has been associated with protection. We found 55.9% to have positive islet cell antibodies (ICA) with 4 of these having a positive complement fixation test. Three patients (7.9%) were found to have positive insulin autoantibodies. No positive serotypes for enterovirus (Coxsackie-B) were found in our patients, but we detected 11 cases with elevated titers for cytomegalovirus antibodies. Positive antibodies for measles, mumps, herpes and varicella were found in some children. This study contributes to a better understanding of the epidemiology and immunogenetics of insulin dependent diabetes mellitus in Latin-American children.