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Selected Abstracts from the 6th Annual Meeting October 18-22, 1992—Las Lenas, Argentina

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1

GROWTH HORMONE RESPONSES TO GROWTH HORMONE RELEASING PEPTIDE (GRP) AND TO GROWTH HORMONE RELEASING HORMONE (GRF) IN GROWTH HORMONE DEFICIENT CHILDREN (GND). V. Mericq, F. Cassorla, H. Garcia, A. Avila, Cy Bowers and G. Merriam. Institute of Maternal and child Research, University of Chile; Santiago, Chile; DEB, NICHD, Bethesda, MD; University of Washingtin, Seattle, WA. and Tulane University, New Orleans, LA.

GH-releasing peptide is a potent and specific stimulator of GH secretion. It is a 6 aminoacid peptide with lower m.w. and loger half life than GRF. To clarify how this peptide acts, we administered separately 1 ug/kg bolus doses of GRP and GRF iv to 29 children (15 M,14 F), ages 3-16 years,with previously documented GHD.Tests were separated by at least 1 week.Bone ages ranged from 1-10 years and growth velocities were less than 3 cm/year. GH responses to 2 indirect GH stimulation tests were less than 7 ng/ml. GH was meassured by RIA with an intraassay cv of 5%. A positive response was defined as a GH increase greater than 4 cv's.We observed 14 (48%) positive responses to GRP,and 18 positive responses to GRF (62%), 9 (31%) patients responded to both peptides. Out of the 14 GRP responders only 9 patients (64%)had a positive response to GRF, and out of the 18 GRF responders only 9 (50%)had a positive response to GRO. GH peak levels were observed between 5 and 60 min (mean 30 min)after GRF,and between 10-45 min (mean 24 min) adter GRP.We conclude that GRP is a potent secretagogue of growth hormone in a substantial proportion of GH deficient children. The dissociated response to GRP and GRF suggests that they stimulate GH release through different mechanisms.

2

GROWTH HORMONE (GH) SPONTANEOUS SECRETION IN CHILDREN WITH SHORT STATURE (SS). A. Martínez, G. Ropelato, JJ. Heinrich, C. Bergadá CEDIE. Div. de Endocrinol. Hosp. de Niños "Dr. Ricardo Gutierres". Buenos Aires, Argentina.

An abnormality in spontaneous GH secretion has been suggested in children with short stature. Twenty eight prepubertal children were studied. Group A: Nine short children, with normal growth velocity and a normal response to provocative tests for GH(≥10 ng /ml),chronological age(CA)(X±SD)9.51±2.95 years,bone age(BA) 7.45 ± 3.84. Group B: 15 children with short stature, subnormal growth velocity and normal GH response, CA 11.39±2.27 and BA 8.98±2.55. Group C:4 children with idiapathic GH deficiency,CA 12.27±3.60,BA 10.6±2.95. Spontaneous overninght GH levels were obtained. GH was measured by RIA.Mean 12 hrs.GH levels(XGH),GH amplitude(A),frecuency (F)and the highest spontaneous GH peak(MxE) were analyzed.

	XGH (ng/ml) (X±SD)	A (ng/ml)	F	No Peaks	MxE (ng/ml)
GA	4.45 ± 1.37	8.45 ± 4.27	4.33 ± 1.0		18.19 ± 9.52
GB	4.09 ± 2.09	9.57 ± 5.09	3.93 ± 1.09		19.13 ± 11.78
GC	1.78 ± 0.52	3.01 ± 2.25	1.75 ± 1.26		4.92 ± 3.11

A correlation between XGH and MxE was found (r=0.79, p<0.001). No correlation between XGH and growth velocity could be observed.The 99 percent confidence limits for XGH in group A were 2.91 to 5.99 ng/ml. Four children of group B had XGH below this limit, with values similar to the children with GH deficiency. In these 4 children the MxE was also below the 99 percent confidence limit. This results suggest a GH secretory disturbance in these 4 children, but not in the other patients of groups B in whom the pattern of secretion did not differ of that of children growing normally.

3

DIRECT ANALYSIS OF THE cP450 21B GENE IN 21-HYDROXYLASE DEFICIENCY (21-OH) USING THE POLYMERASE CHAIN REACTION (PCR). A. Dardis and A. Belgorosky. Laboratorio de Investigación, Hosp. J. P. Garrahan, Buenos Aires, Argentina.

In humans two 21-OH genes with high homology are present: A (inactive) and B (active). A modification of PCR which amplifies specific alleles, would allow for specific amplification of the active gene. The purpose of the present study was to develop a PCR technique for detection of partial or total cP450 21B gene deletions or gene conversions. These abnormalities accomit for 25% reported abnormalities in other populations. DNA template was extracted from peripheral leucocytes (3ml blood samples). For PCR 500 ng template, 2.5 U Taq I polymerase, 4mM MgCl2 and 0.2uM of 2 oligonucleotides (primers) were mixed. These primers will amplify 300 pB of Exon 3, Intro 3 and a fraction of Exon 4 for cP450 21B. Thirty five cycles (denaturation 1 min at 93o C, hybridization 2 min at 60o C and extension 3 min at 72o C) were carried out. Amplification of B-globin gene was used as control. The amplified product was analyzed by 1% agarose gel electrophoresis with ethidium bromide in the presence of molecular weight standards. Ten patients with CAH (6 salt losers) and ten normal control (C) were studied. cP450 21B was amplified in 9/10 patients and in the 10 C. The patient in whom cP450 21B was not amplified, the B-globin was normally amplified. This patient was a salt loser. It is concluded that the method can show partial or total gene deletions, as well as gene conversions, in 21-OH deficiency. Point mutations probably require restriction enzymes analysis of the amplified product.

4

GONADOTROPIN SECRETION IN CONGENITAL ADRENAL HYPERPLASIA (CAH). ME. Escobar, H. Domené, G. Ropelato, L. Gruñeiro, C. Bergadá. Div.de Endocrine Hosp. de Niños R. Gutierrez. Bs.As., Argentina.

Menstrual disorders are frequent in women with CAH. With the purpose to analyze the effect of the hyperandrogenism on gonadotropin secretion, we have studied 12 women with 21 hidroxilase defiency,X age 19.3years;six had amenorrhea,4 oligomenorrhea and 2 were eumenorrheic. One of them had never received treatment, 2 stopped treatment 2-3 years before and 9 were on corticoid replacement. Serum E2, 17OH progesterone (17 OHP), urinary 17-Ketosteroids (17-KS)and pregnanotriol (triol),and spontaneous LH and FSH levels every 20 minutes during 12 nocturnal hours (5 studies) or 4-6 diurnal hours (8 studies),were measured.Results: Three patterns of gonadotropin secretion were detected:1)Apulsatile,n=7: X LH 1.2±0.3 IU/L; 2)Low pulsatility n=4: X LH 2.7±1.1 IU/L,X pulse amplitude (P.A.) 3.2±1.6, X pulse frecuency (P.F.) 0.23±0.08 p/hour;3) Normal pulsatility n=2 X LH 7.6 IU/L, P.A. X 4.9 IU/L, P.F. X 0.43 p/hour.No correlation was observed between gonadotropin levels and 17OHP, 17-KS or triol at the moment of study;a weak(ns)correlation was found with those values1-2 years before the study.Two patients with optimal corticoid replacement since birth, and two untreated patients presented an apulsatile gonadotropin secretion pattern. Conclusion: CAH due to 21 hydroxylase deficiency is associated with variable degrees of impaired gonadotropin secretion,even in patients with adequate corticoid treatment, suggesting an hypothalamic alteration as a consecuence of the prenatal exposure to high androgen levels.