0031-3998/84/1811-0000$02.00/0
PEDIATRIC RESEARCH

Vol. 18, No. 11, 1984
Printed in U.S.A.

Abstracts

23RD ANNUAL MEETING

EUROPEAN SOCIETY FOR PAEDIATRIC ENDOCRINOLOGY

Heidelberg, Germany, September 2–5, 1984

President: Dieter Schönberg, Germany
Secretary: Albert Aynsley-Green, United Kingdom
Treasurer: Michel L. Aubert, Switzerland
Council: J.L. Chaussain, France
A. Larsson, Sweden
W.G. Sippell, Germany
M. Vanderschueren-Lodeweyckx, Belgium

1 M.GOOSSENS*, P.DUQUESNOY*, R.AMIRA*, P.CZERNICHOW, R.RAPPAPORT. INSERM U91 Créteil, and INSERM U30 Hôpital des Enfants Malades, Paris. France.

Growth hormone deficiency type A due to a novel deletion in the hGH gene cluster.

A hGH gene deletion has been reported only in patients with type A complete GH deficiency. We had the opportunity to examine 12 children with isolated GH deficiency (10 boys and 2 girls) belonging to 6 families. In 10 cases (5 families) peak plasma GH after AITT varies between 0.9 and 7 ng/ml and were treated with some succes by hGH. Two boys (1 family) had autosomic recessive type A GH deficiency and produced high titer hGH antibodies shortly after onset of hGH administration that was unsuccessfull. DNA from the patients and family members was studied by restriction endonuclease analysis with a ^{32}p labelled hGH cDNA probe. Analysis of the restriction pattern obtained in both parents and in the type A dwarfs showed the existence of an extensive deletion involving more than 40 kb of the GH gene cluster. The two children were homozygous for this deletion which left intact the hCS-L gene, removing on the 5' side the hGH-N gene, and on the 3' side the hCS-A, hGH-V and hCS-B sequences. No deletion was found in the other families.

In conclusion, the present results are different from the deletions previously reported by Phillips et al, and further demonstrate the genomic heterogeneity of the familial isolated growth hormone deficiency type A.

2 M.L. AUBERT, M. BEGEOT*, B.P. WINIGER*, G. MOREL*, P.C. SIZONENKO, and P.M. DUBOIS*. University of Geneva School of Medicine, Switzerland, and University of Lyon-sud, Oullins, France.

Ontogeny of hypothalamic GnRH and pituitary GnRH receptors in fetal rats.

In order to clarify the different roles of GnRH during fetal life, the first appearance of GnRH in the fetal brain, the expression of GnRH receptors on the fetal pituitary gland, and the presence of GnRH within the fetal gonadotrophs have been investigated. GnRH was present in the earliest brain examined (12 days of gestation). From 12 to 17 days, GnRH content of fetal brain remained low and then increased markedly by the end of gestation. No immunoreactive GnRH-like material could be detected in placental tissue throughout gestation. Binding sites for GnRH were detected as early as 12 days of gestation in fetal pituitary gland. At 17 days, Scatchard analysis indicated the presence of high affinity, low capacity binding sites. Intracellular presence of GnRH as seen by immunocytochemistry was first visible at 14 days and started to increase at 16 days. LH was first detectable in the fetal pituitary at 17 days, and FSH, at 21 days. In summary, hypothalamic GnRH appears very early in fetal life and potentially can induce differentiation of the pituitary anlage. Conversely, the presence at 15 days of gestation of specific binding sites for GnRH and of intracellular GnRH immunoreactivity in gonadotrophs indicates that the hypophysiotropic action of GnRH clearly precedes the start of LH biosynthesis.

3 M. JANSEN*, H.H.M. VAN TOL*, F.M.A. VAN SCHAIK*, J.L. VAN DEN BRANDE, J.S. SUSSENBACH*. Depts. of Pediatrics and Physiological Chemistry, State University of Utrecht, the Netherlands.

Human insulin-like growth factors I and II (IGF-I, IGF-II) are synthesized as precursors.

In an attempt to further investigate the structure of the Somatomedins/Insulin-like Growth Factors (SM/IGF), especially the possible existence of precursor peptides and their structural relation to the circulating forms, we have used recombinant-DNA techniques to identify and isolate cDNA-clones encoding human IGF-I and -II.

By screening an adult human liver cDNA-library with a synthetic oligonucleotide, we initially isolated a cDNA encoding the 70 amino acids of IGF-I preceded by an N-terminal peptide of at least 25 amino acids and a carboxyl-terminal peptide of 35 amino acids, thus demonstrating that IGF-I is synthesized as a precursor. Subsequently, by cross-hybridizing the cDNA-library with restriction fragments of this cDNA we were able to isolate another cDNA clone, encoding the 67 amino acids of IGF-II, flanked by nucleotide sequences encoding a highly hydrophobic leader peptide and a carboxyl-terminal peptide.

These results provide solid evidence that both IGF-I and IGF-II are synthesized as precursor proteins and that formation of IGF-I and IGF-II from these precursors requires proteolytic processing at both the N-terminal and the C-terminal ends.

4 A GROSSMAN*, M O SAVAGE, A BLACKLAY*, N LYTRAS*, P N PLOWMAN*. M A PREECE, D H COY* and G M BESSER*. Departments of Endocrinology, Child Health and Radiotherapy, St Bartholomew's Hospital, London EC1, Institute of Child Health, London WC1, and Department of Medicine, Tulane University, New Orleans, Louisiana, USA.

Responses of serum GH and somatomedin-C to an analogue of GHRH in children with growth hormone deficiency.

Twenty-seven children and young adults with growth hormone deficiency (GHD) were given an i.v bolus of 200 ug of either GHRH(1-40) or of a shorter analogue of growth hormone-releasing hormone, GHRH(1-29)NH_2; serum GH and somatomedin-C levels were measured. Thirteen showed a significant rise in serum GH, including 3 patients with hypothalamic tumours, 7 with idiopathic isolated GHD or panhypopituitarism and 3 children cranially-irradiated for non-endocrine tumours. A poor response was seen in patients with isolated GHD who had been on long-term therapy. Four patients given a second dose of 500 ug GHRH(1-29)NH_2 two hours after the first dose showed little response to this second dose. Long-term (8-24 hr) i.v infusion of GHRH(1-29)NH_2 demonstrated pulsatile GH secretions with no evidence of priming or down-regulation. Somatomedin-C levels, when measured, rose in parallel to serum GH, and often became normal. It is concluded (i) that children with idiopathic GHD, hypothalamic tumours, and cranial irradiation may have a defect in the synthesis or delivery of endogenous GHRH; (ii) GHRH(1-29)NH_2 is a useful test for pituitary GH reserve in such patients; (iii) GHRH(1-29)NH_2 may have long-term therapeutic potential.