59

D.B. Dunger* J.Seckl* S.Lightman* (introd. by
Hospital for Sick Children, Great Ormond Street, and the Charing Cross and Westminster Medical School. London.

NEUROHYPOPHYSEAL FUNCTION IN EARLY POST-OPERATIVE DIABETES INSIPIDUS.

Diabetes Insipidus (DI) following surgery to the pituitary or hypothalamus may be transient, prolonged or show a triple response.

We have investigated 11 children (1.8-15 yrs) following such surgery. Plasma vasopression (AVP), human neurophysin I (HNPI) and oxytoxin (OT) concentrations were determined at the onset of DI and daily thereafter. Water deprivation tests were performed on day 6 and 14. All had corticosteroid and thyroxine replacement.

9 patients developed early post-op DI (onset 1-12 hrs). Initial plasma AVP levels were high 3.9 ± 1.2 pmol/L and fell to 1.1 ± 0.2 pmol/L by the 2nd day ($P<0.05$) HNPI concentrations also fell from 0.7 ± 0.2 ng/ml to 0.2 ± 0.1 ng/ml ($P<0.05$) whereas plasma OT levels remained unchanged. HPLC performed on day 1 plasma revealed a major peak co-eluting with synthetic AVP and two smaller peaks of immuno reactivity.

Water deprivation tests showed no differences between patients with a triple response or uninterupted DI. Taken together, final plasma AVP concentrations on day 6 (0.8 ± 0.5 pmol/L) were similar to those on day 14 (0.5 ± 0.1 pmol/L). Maximal urinary AVP excretion on day 6 (2.4 ± 0.8 pmol/hr) was significantly ($P<0.05$) greater than on day 14 (0.7 ± 0.3 pmol.hr).

Early post-op DI is not due to reduced circulating AVP but may be related to release of biologically inactive procursors.

The difference in urinary AVP excretion between days 6 and 14 is insufficient to explain the resolution phase of the triple response.

60

P. Adlard*, Y. Yi-Yan*, F. Buzi*, J. Jones*, M.A. Preece
Department of Growth and Development, Institute of Child Health, London, England.

PULSATILE PROLACTIN SECRETION IN HYPOTHALAMIC-PITUITARY DISORDERS

We have studied nine children with a variety of hypothalamic pituitary disorders and delayed puberty, before and during nocturnal pulsatile GnRH therapy given subcutaneously in a dose of 2 - 4 µg every 90-120 minutes. Initial age ranged from 13.5 - 18 years. The duration of therapy was >0.5 years. Overnight serum profiles of prolactin, growth hormone and gonadotrophins were obtained by blood sampling at 15 minute intervals.

In the three severely growth hormone deficient patients there were very low levels of prolactin (0-150 mIU/L), without appreciable pulsatility or sleep-related rise. In the remainder there was no clear relationship between prolactin levels and GnRH or gonadotrophin pulses. In those patients with normal growth hormone secretion, including two with isolated gonadotrophin deficiency, there was a temporal relationship between growth hormone and prolactin pulses.

These results therefore seem to contrast with data from adult studies, in that pulsatile prolactin secretion was more related to growth hormone status and release than to GnRH or gonadotrophins. This may have important implications for our understanding and management of hypothalamic-pituitary disorders.

61

M Charlesworth*, R J M Ross*, A Grossman*, J A H Wass*, G M Besser*, M O Savage
Departments of Child Health, Endocrinology and Neuroradiology, St Bartholomew's Hospital, London UK

ENHANCING HYPOTHALAMIC LESIONS SHOWN ON HIGH RESOLUTION COMPUTERIZED TOMOGRAPHY IN PATIENTS WITH IDIOPATHIC HYPOPITUITARISM

No cause is defined in the majority of children with hypopituitarism and they are labelled as 'idiopathic'. Five patients 3 boys and 2 girls, aged from 2 to 22 years, underwent high resolution (GE9800) CT scans of the hypothalamic and pituitary regions. Four had pan-hypopituitarism, 1 with diabetes insipidus and 1 had isolated GH deficiency. Peak GH responses to hypoglycaemia (ITT) or glucagon were less than 5 mU/l and after bolus GHRH (1-29)NH2 in 3 patients, GH was 11.8, 11.5 and 10.2 mU/l, indicating hypothalamic GHRH deficiency. In 1 patient peak cortisol during ITT was 275 nmol/l compared with 690 nmol/l after bolus CRF 1-41 infusion. Prolactin levels were elevated in all subjects ranging from 562 to 1329 mU/l (normal value less than 360 mU/l). In each case CT scan demonstrated a definite enhancing lesion in the anterior hypothalamus, situated in the floor of the third ventricle, adjacent to the chiasm or in the region of the tuber cinerium. In 4 patients the pituitary gland was small. Biopsies were not performed. Repeat scan after 18 months in 2 subjects showed no change. Thus apart from hypopituitarism, the lesions produced no symptoms. We suggest that these may be of aetiological significance, correlating with endocrine evidence of hypothalamic dysfunction.

62

R.Brauner*, V.Barral*, R.Reppaport, D.Lallemand*.
Department of Pediatric Endocrinology and Diabetes, INSERM U.30, Department of Radiology, Hôpital des Enfants-Malades, 149, rue de Sèvres, 75015 Paris, FRANCE.

MAGNETIC RESONANCE (MR) AS AN ADDITIONAL DIAGNOSTIC TOOL FOR HYPOTHALAMIC HAMARTOMA.

Hypothalamic hamartoma (HH) is assumed to be made of normal neuronal tissue ectopically located, and is often associated with true precocious puberty (PP). Its recognition is of great importance as this tumor does not require irradiation and is generally not invasive. Diagnosis is based on the following criteria : 1) the localisation to the floor of 3rd ventricle ; 2) the CT scan appearance as a mass isodense to gray matter before and after injection of contrast media ; 3) the absence of elevated circulating levels of hCG and α-fœto-protein ; 4) the lack of extension on follow-up. The contribution of MR was investigated in 7 cases (6 with PP and 1 with gelastic epilepsy). In 6 out of 7 cases the tumor signal was compared to that of gray matter : 1) it was identical on T_1 weighted images ; 2) but it was superior on T_2 indicating some structural difference. A hamartoma like structure was found at biopsy in one of these cases. The last case showed a signal intensity identical to normal cerebral tissues.

In conclusion, these MR data provide a new diagnostic tool in addition to the other biological, clinical and CT scan data. They also suggest that HH might have a structure different than normal brain tissues.

63

J.Argente[x], D.Evain Brion, P.Garnier, M.Hernandez[x], M.Donnadieu[x], J.C.Job
INSERM U 188, 75014 Paris, France, Fondation de Recherches en Hormonologie, 94260 Fresnes

RELATIONSHIP OF PLASMA GROWTH HORMONE RELEASING HORMONE (GHRH) LEVELS TO PUBERTAL CHANGES

Basal plasma GHRH levels were determined by RIA, as previously described, (Donnadieu, JCEM 60:1132, 1985) after an overnight fast in 93 normal boys and 87 normal girls aged 8 to 18 years. Sixteen boys with idiopathic delayed puberty (IDP) were also studied. Plasma GHRH levels increased above prepubertal values during the teenage years. At mid-puberty GHRH levels in girls (mean ± SEM) were 159.1 ± 28.5 pg/ml, 5 fold the prepubertal values (30.0 ± 4.3), and in boys 101.4 ± 11.5 pg/ml, 2 fold the prepubertal values (48.1 ± 5.2). Basal GHRH levels of boys with IDP were significantly lower (20.5 ± 5.2 pg/ml). In addition, boys with IDP presented a failure of response of plasma GHRH after L-Dopa stimulation. The sharp rise of plasma GHRH levels during puberty in both sexes suggests a role for this peptide in the adolescent growth spurt. The low basal GHRH levels and its impaired release after L-Dopa stimulation in IDP suggest a possible hypothalamic dysfunction in this syndrome.

64

H. Kinarti*, R. Keret*, Z. Josefsberg*, B. Szoke*[1], A.V. Schally*[1], Z. Laron. Inst. Ped. Adolesc. Endocr. Beilinson Med. Ctr., Petah Tikva, Sackler Med. Sch. Tel Aviv Univ., Israel & Polypeptide Lab.[1], Tulane Med. Sch., New Orleans, L.A., USA.

hGH RESPONSE TO REPEATED GH-RH 1-44 ADMINISTRATION IN HYPOPITUITARY CHILDREN

The aim of the present investigation was to determine the effectiveness of 1 daily s.c. injection for 5 consecutive days of GH-RH 1-44 (1 mcg/Kg) on the plasma hGH response to an i.v. bolus of GH-RH 1-44 (1 mcg/Kg) in hypopituitary patients who had a subnormal response of plasma hGH to previously performed tests: ITT, clonidine, sleep. The i.v. GH-RH test was performed before (I) and day after (II) the last i.m. injection.

Eleven children (7 IGHD, 4 MPHD) were studied. According to the results the patients were sub-divided into 3 groups:

GR	n	CA	BA	Peak Plasma hGH ng/dl I. GH-RH	II.GH-RH	p
I	4 (1M+3F)	13.0±4.9	9.9±3.7	11.7±4.9	22.9±7.3	.05
II	5 (4M+1F)	8.9±2.6	6.1±4.1	12.6±4.0	13.2±5.3	NS
III	2 (2F)	7.5±3.3	5.0±3.1	2.5±0.8	2.8±0.7	NS

In GR I 3 girls were in puberty and the peak response of hGH to other tests was 5.1±1.9. In GR II 4 boys were prepubertal, had a lower peak of hGH in other tests 2.3±0.9, whereas in GR III there was no rise in any test. This investigation indicates a) that repeated administration of GH-RH even in small doses is useful in the differentiation of patients who may benefit from prolonged therapy; b) that hGH responsiveness to GH-RH may be influenced by sex hormones.