43 B. SCHNEIDER*, L. LEVINE*, A. ROSLER*, S. OBERFIELD*, E. FORSTER*, and M. NEW, Rockefeller Univ. & Cornell Univ. Med. Col., NewYork

Hyperaldosteronism with non-suppressible ACTH

In an 11 yr old male with the syndrome of primary hyperaldosteronism and hypertension due to adrenal hyperplasia, we have found evidence for abnormal ACTH regulation. Since renin is completely suppressed, it is not regulating aldosterone. Diurnal periodicity of F was normal and F, DOC and B were normally stimulable with ACTH and suppressible with dexamethasone. In contrast, though aldosterone was stimulable with prolonged ACTH administration it was not suppressible with high-dose, long-term dexamethasone. Circulating ACTH levels were repeatedly elevated and were also non-suppressible with dexamethasone despite complete suppression of F, DOC and B. The data suggest the presence of two hypothalamic-pituitary systems, one regulating F in the normal fashion, the second involving a species of non-suppressible ACTH which presumably does not regulate F secretion. Preliminary characterization of the patient's ACTH showed that it is of a higher molecular weight than the normal ACTH 1-39. Whether chronic elevation of this form of ACTH is related to the hyperaldosteronism and adrenal hyperplasia or, indeed, is the cause of selective hypersecretion of aldosterone in this patient is under investigation.

44 J.P. BOURGUIGNON*, C. LEINARTZ-DOURCY*, C. HOYOUX* and P. FRANCHIMONT* (Intr. by R. Wolter)

Clinique des Maladies de l'Enfance et Laboratoire de Radioimmunologie (Institut de Médecine). Hôpital de Bavière, Université de Liège, Belgium.

Urinary excretion of LH-RH-like material from birth to puberty.

Endogenous LH-RH-like material was radioimmunoassayed in human urine, after extraction by silicate and methanol. This material was shown to be related to LH-RH by its immunological, physicochemical and to a lesser extent, biological properties : using 3 antisera with different affinities for LH-RH C- and N- terminals, the extracted material appeared heterogeneous and contained slight decapeptide-like immunoreactivity. This decapeptide-like material showed on sephadex a chromatographic similarity to rat hypothalamic extracts and to the unextracted material excreted in urine after intravenous injection of synthetic LH-RH. Whilst adult values of urinary decapeptide-like material ranged from 4 to 30 ng/day, the excretion was lowest in infants up to the age of 3 months ($< 1,5$ ng/day). From 1 to 6 years, the observed values were less than 4 ng/day. From the age of 7, some higher values were found, suggesting a possible role of LH-RH in the initiation of puberty.

45 W.RAUH*, L.LEVINE*, E.FORSTER* and M.NEW, Div.Ped. Endocrinol., Cornell Univ.Med.Coll., New York, USA.

Aldosterone metabolism after prolonged ACTH administration in juvenile hypertension.

The effect of a 5-day continuous ACTH infusion (Acthar, 40 U/24h) on aldosterone metabolism was evaluated in 3 hypertensive children with hyperaldosteronism, 2 children with essential hypertension, and 1 normotensive control. Plasma aldosterone concentration (PA) and urinary excretion of aldosterone pH1 conjugate (pH1A), tetrahydroaldosterone (THA) and free aldosterone (FA) were measured by radioimmunoassay. In the patients with hyperaldosteronism, PA rose 3-fold and the 3 urinary metabolites showed a sustained 5-fold increase throughout the ACTH test. In the other children, PA and urinary aldosterone metabolites rose 2-4 fold on the 1st day of ACTH administration, but decreased on the 4th and 5th day. pH1A fell more rapidly than either THA or FA. Consequently, the THA/pH1A ratio rose from 3.0 to 8.6 during the 5-day ACTH test. Conclusions: 1) prolonged ACTH administration induces a shift in the excretory pattern of the aldosterone metabolites leading to increased excretion of THA and FA; 2) pH1A alone is not an adequate index of aldosterone secretion in prolonged ACTH administration; 3) in hyperaldosteronism, ACTH produces an unusual sustained increase of all aldosterone metabolites.

46 I.A. HUGHES* and J.S.D. WINTER* (Intr. by C.G.D. Brook).

Tenovus Inst., W.N.S.M., Cardiff and Health Sciences Centre, Winnipeg, Canada.

Steroid interrelationships in congenital adrenal hyperplasia (CAH)

17-Hydroxyprogesterone (17P), testosterone (T), androstenedione (A), progesterone (P), 17-ketosteroids (17KS) and prenanetriol (p'triol) were measured serially in 31 CAH patients. Infants and adolescent girls showed significant correlations between 17P and T, A, P, respectively ($p < 0.001$). A 17P $<$200ng/dl (6nmol/l) was associated with normal T, A, and P levels. A 17P 200-1000ng/dl (6-30nmol/l) produced occasional abnormal levels; when $>$ 1000ng/dl (30nmol/l), other steroid levels were high (particularly p'triol). There was no correlation between 17P and T in adolescent males ($p > 0.25$). In infants, there was a significant correlation between mean 17P and T and height velocity SDS ($p < 0.01$). First year height velocity showed a significant negative correlation with hydrocortisone dose ($p < 0.01$). The results show the benefit of serial 17P and T measurements in the longer term management of CAH.

47 R.A. HARKNESS* and D. THISTLETHWAITE* (Intr. by D.B. Grant). Departments of Paediatric Biochemistry and Child Life & Health, University of Edinburgh, EH9 1LJ, UK.

Delayed puberty in adrenocortical hypoplasia.

Delayed puberty was apparent at age 15 years in a boy with congenital adrenocortical hypoplasia, a diagnosis initially suggested by an autopsy on a newborn male sib. The diagnosis was confirmed from elevated plasma ACTH, 1462ng/l, and low urinary 17-OHCS, 0·4mg/24h. Plasma testosterone was low and there was only a three fold increase in response to HCG. FSH concentrations were higher than LH and both were prepubertal; the response to LRF was sluggish. Cortisone acetate was increased to 25mg/day and 0·1mg fludrocortisone added; growth and pubertal development were regularly measured but no androgenic treatment given. In 6 months, the plasma testosterone had risen to 4·6nmol/l, in addition the LH concentration had increased to 3·8u/l and was responsive to LRF. Pubertal development was definite after 12 months. A similar delay occurred in a relative (Dr. Rowan, Glasgow). The means by which the adrenal cortex aids the testes in its responses including pubertal development, is not known although metabolic cooperation in steroid biosynthesis appears probable.

48 *F. HADZISELIMOVIC*, J. GIRARD and B. HERZOG* (Intr. by J. Girard) Univ. Children's Hospital, Basel, Switzerland.*

Further support for a gonadotrophine deficiency in cryptorchidism derived from clinical investigations.

In 73 uni- and bilateral cryptorchid boys (2-13 years of age) LH and FSH response to LH-RH (or long acting LH-RH derivative HOE 766) was assessed. In all patients a testicular biopsy -taken during orchidopexy- was examined by light and electronmicroscopy. Plasma LH increased from 3,5 to 10,1 mU/ml and FSH from 1,5 to 4,5 mU/ml in response to 100 ug LH-RH, testosterone (mean 0,48 ng/ml) and E2 (mean $<$ 30 pg/ml) did not increase significantly. In 34/73 patients the LH concentration rose to $<$ 4 mU/ml above the basal value, in 11 plasma LH was not stimulated at all. A pronounced stimulation of FSH of $>$ 4 mU above basal concentration was seen in 30/73 boys. In all biopsies of patients with no LH response, Leydig cells were spare in the interstitium. Collagenization of interstitium and of peritubular connective tissue could not be related to LH and FSH. Unequivocally the number of spermatogonia was reduced and their ultrastructural appearance pathological.