143

U.Willi*, M.Atarés*, A.Prader, M.Zachmann
Div.of Radiology and Dept.of Pediatrics, University Children's Hospital, Zürich, Switzerland

TESTICULAR ULTRASONOGRAPHY (US) DEMONSTRATING HETEROTOPIC ADRENAL-LIKE TISSUE (HALT) IN PATIENTS WITH CONGENITAL ADRENAL HYPERPLASIA (CAH)

HALT has been reported in male pts with CAH. We have examined 15 male adolescents and young adults with CAH aged 11.9 -36 yrs. Size, shape and firmness of the testes were assessed clinically and US was performed at least once in each pt. Seven pts, all under long standing treatment with glucocorticoids, showed abnormal results by US (group I); and 8 pts, 5 under treatment and 3 off treatment for several yrs, showed normal results (group II). In group I testes had normal volume (9-15ml), felt hard and had irregular shape. On US there was an abnormal heterogeneous pattern. Sperm count obtained in 3 pts was 5.0 to 17.4 x 10^6/ml. Biopsy in 1 pt confirmed the presence of HALT. Five pts have 21-hydroxylase deficiency diagnosed in early infancy because of manifest salt loss; 2 pts have 11-β-hydroxylase deficiency diagnosed late (2 and 5 yrs). In group II testicular volume (6-18ml), shape and firmness were normal, and US revealed a normal homgeneous pattern. All pts have 21-hydroxylase deficiency, no history of salt loss and were diagnosed late (3-7 yrs). Sperm counts in 3 pts off treatment were 10.5, 20.0 and 66.0 x 10^6/ml. Conclusions: US shows HALT objectively. HALT with deficient spermiogenesis is frequent in male adolescents and young adults with salt loss, even under treatment. In mild cases, HALT is absent, spermiogenesis may be nl, even off treatment.

144

R.P.Willig, M.Kleij+, D.Börger+, A.Lassrich+
Dept. of Pediatrics, University of Hamburg, FRG

DIFFERENCES BETWEEN PHALANGEAL AND CARPAL BONE MATURATION IN CONGENITAL ADRENAL HYPERPLASIA (CAH)

Determinations of bone age (BA) in CAH often reveales discrepancies between phalangeal (pBA) and carpal BA (cBA). To elucidate this observation we followed the BA of 38 girls and 15 boys with CAH using the methods of Tanner and Whitehouse (Carpal, RUS, TW 2o) and of Greulich and Pyle (GP). Bad treatment resulted in significant acceleration of pBA, while cBA correlated well with chronological age (CA). Therefore the method of GP, which does not differentiate between pBA and cBA, has difficulties in determing an exact BA if CAH-children are accelerated. Applying the GP-method to such cases one should look onto pBA rather than onto cBA. It is supposed that the dissociated development of BA is due to the different growth of phalangeal and carpal bones (epiphysial and enchondral ossification).

		girls				boys			
CA:	$\bar{x}$	6.33	8.23	1o.1o	12.o4	6.17	8.28	9.91	11.95
Carpal:	$\bar{x}$	6.61	8.19	1o.28	11.83	7.15	8.75	1o.28	12.o6
RUS:	$\bar{x}$	7.19	9.34	11.64	13.33	8.53	1o.58	12.o8	13.3o
TW 2o:	$\bar{x}$	6.77	8.62	1o.8o	12.46	7.7o	9.58	11.13	12.59
GP:	$\bar{x}$	7.o4	8.9o	11.13	12.45	7.84	9.81	11.o6	12.42

Tab.: BA-determinations (years) in girls and boys with CAH of different age groups (◂ = significant differences, p<o.o1)

145

J.B. Baumann*, J. Girard, A.N. Eberle* (introduced by J. Girard)
Children's Hospital, and Dept. of Research, University of Basel, Switzerland

AGE-DEPENDANT VARIATION IN FUNCTION OF THE ADRENAL CORTEX IN RATS

Proopiomelanocortins (POMC) secreted concomitantly with ACTH may be involved in control of adrenal growth and function with changing needs for POMC peptides during development. This might explain an increased ACTH response to stress, which was found in 2-4 week old, compared to adult rats. Therefore, the sensitivity of the adrenal to ACTH was compared between prepubertal (pp)(25 days) and young adult (ya)(70 days) rats. In vivo: In dexamethasone-blocked rats, corticosterone (c) 20 min after 25 ng $ACTH_{1-24}$/100 g bw i.v. was significantly higher (50.3±2.1 ng%) in pp compared to ya rats (41.0±1.8 ng%). In contrast, 5 ng ACTH/100 g bw could not stimulate c in pp (4.8±1.6 ng%), but markedly in ya (30.8±1.7 ng%). For a comparable c-response in pp rats, 10 ng of ACTH/100 g bw was required. In vitro, cells prepared by collagenase dispersion from inner zones of the adrenal cortex, revealed similar results: 1 pg of ACTH elicits a significant response in ya, but 5 pg are needed in pp rats. ED_{50} was correspondingly increased from $2x10^{-12}$ M to $1x10^{-11}$ M. Maximal responses were similar and dose response curve parallel. This suggests a protective mechanism against an over-production of c, due to large amounts of ACTH released with other POMC-peptides needed for adrenal growth in prepubertal animals.

146

*C.Terzi,*D.Krüger(introd.by A.Attanasio),A.Attanasio S.Bernasconi,G.Giovanelli and D.Gupta,Dept.of Diagnostic Endocrinology,University Childrens Hospital,Tübingen, FRG,and Pediatric Clinic,University of Parma,Italy

CIRCULATING POLYMORPHIC FORMS OF ACTH AND RELATED PEPTIDES:AGE-DEPENDENT NATURE OF DEXAMETHASONE SUPPRESSION IN MALE RATS

Proopiomelanocortin(POMC) through post-translational processes gives rise to a series of structural related peptides.These include MSHs,ACTHs,CLIPs,LPHs,and endorphins.In this study we have examined various molecular forms of ACTH-like immunoreactivity(ACTH-LI) present in systemic blood of male rats by chromatofocusing.To gain further insight into the physiological basis of the release of ACTH-LI peptides and its age-dependent nature,we have studied various molecular forms of ACTH-LI under dexamethasone(DX),which is expected to inhibit the release of endogenous CRF.Resolution of circulating ACTH-LI peptides utilizing chromatofocusing revealed 6 heterogenous components having isoelectric points between 4.7and 3.29.The results demonstrated entirely different patterns of ACTH-LI peptides seen in the prepubertal group and the adult group. While the prepubertal pattern showed a relative shift to less acidic components,the adult animals had more acidic components.Under DX less acidic components in the prepubertal group were diminished and acidic components were increased.In the adults the less acidic components did not show any alterations,while the more acidic component (peak VI) was greatly enhanced.With these studies as a baseline,it convincingly demonstrates that the alterations in the ACTH-LI components with maturation are perhaps involved in the biopotency of a hormone,and inhibition of CRF by DX modulates the shift of the components from less acidic to more acidic forms.

147

S.Bernasconi, F.Facchinetti*, C.Marcellini, S.Mari, L.Ghizzoni, A.R. Genazzani*.
Department of Pediatrics and Obstetrics*, University of Parma and Modena*, Italy

BETA ENDORPHIN (B-EP) and CORTISOL (C) RESPONSES TO CRF IN OBESE ADOLESCENTS.

B-EP and C serum levels in response to CRF were studied in 10 obese adolescent subjects (4M,6F) 8-17 years of age. All patients were healthy with an overweight ranging from 35 to 95% and a mean duration of obesity of 10 years. Blood samples were drawn before and 15,30,60,120,240 minutes after i.v. injection of 1 ug/kg of CRF (CRF Bissendorf). The baseline B-EP and C levels were 12.9 ± 6.3 fmol/ml and 9.4 ± 4.7 ug%ml respectively, confirming the hyper B-EP previously reported. Among these subjects 2 different groups were identified, based on their responses to CRF: A) Responders with 100% increase of B-EP (Δ = 14.4 ± 5.9, n= 4) and B) Non-responders in which B-EP did not rise after CRF stimulation (maxΔ = 1.7, n=4). Furthermore, the mean baseline values of B-EP in group A were significant lower than those in group B (8.17±2.5 v.s. 19.3±4.3 $p < 0.01$). No correlation was found between basal and stimulated levels of B-EP and C in the two groups. These data show that among obese patients 2 different population can be identified based on B-EP responses to CRF and that this distinction is independent from age, sex, % overweight, duration of obesity and C responses.
The significant difference between baseline levels in the two groups suggests that in group B the lack of response to CRF can be related to a chronic overstimulation with either secondary depletion of the reserve capacity or oversaturation of the receptors.

148

Beaufrère B.*, Chatelain P.*, Sassolas G.*, Morel Y.*, Catbeh N.*, Aguercif M.*, Bey-Omar F.*, François R.
Department of Pediatrics, Hopital Ed. Herriot - LYON - France.

CUSHING'S SYNDROME BY ECTOPIC ACTH SECRETION : EFFECT OF MIFEPRISTONE.

Mifepristone (RU 486 - Roussel-Uclaf), an antiglucorticoïd receptor with no agonist activity, has been proposed as treatment of hypercortisolism in adults. A 27 month old girl presented a Cushing's syndrome, ongoing for the past 12 months. She exhibited obesity, delayed growth, moon facies and severe hypertension (200 mm Hg). Urinary free cortisol (UFC) (6275 nmol/day), plasma cortisol (C) (2435 nmol/ml) and ACTH (2016 pg/ml) were elevated and did not respond to dexamethasone suppression test. Plasma CRF was undetectable. Cranial CT scans were normal. The very high ACTH levels were consistent with an ectopic ACTH secretion although its origin could not be located on repeated extensive investigations. RU 486 was administered for 2 months at increasing dosages (5 to 25 mg/kg.d) The patient improved dramatically, lost 3 kg and normalized her blood pressure. UFC (118 nmol/day), C (595 nM) and ACTH (233 pg/ml) all decreased. No side effect was observed. Six weeks after discontinuation of RU 486, there was no clinical evidence of relapse, and UFC (147 nmol/day), C (418 nmol/ml) and ACTH (397 pg/ml) were unchanged. Although spontaneous cure or intermittent ACTH secretion cannot be excluded, this observation could suggest a therapeutic effect of RU 486 on ectopic ACTH secretion. However, its mechanism remains unclear since we observed a fall of cortisol and ACTH, contrary to what has been previously described in adult Cushing's syndrome treated with RU 486.