47

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Adrenal androgens are highly stimulated during ACTH therapy for infantile spasms.

Adrenocortical steroid secretion was studied in 10 infants (mean age 8.9 months, range 5-22 months) during and after ACTH therapy for infantile spasms. Long-acting ACTH (Acortan prolong.®, Ferring, Sweden) was given i.m. once daily, 80 units during the first 3 weeks, 40 units during the following 2 weeks with tapering and termination within the next week. Serum dehydroepiandrosterone (DHA), androstenedione (A) and cortisol (F), and 24 h urinary cortisol (dUF) and 17-ketogenic steroids (KGS) were measured before, during (serum samples 24 h after the last ACTH dose) and after therapy (means and range nmol/l for serum steroids, nmol for dUF and umol for KGS):

	Before	ACTH 3 wks	ACTH 6 wks	2wks after ACTH
DHA	8.2(4.3-12.6)	18.8(4.5-26.9)	15.7(5.0-45.7)	8.9(5.6-10.7)
A	0.9(0.5-1.8)	8.9(1.0-50.4)	5.0(0.4-15.5)	1.1(0.4-2.1)
F	844(193-2250)	1339(152-4140)	1691(5 - 3920)	321(189-596)
dUF	126(13-637)	9897(1578-35000)	4473(812-10800)	17(3 - 80)
KGS	5.7(2.8-19.5)	55.5(13.6-144)	32.1(11.0-79.8)	1.8(0.5-4.1)

Highly elevated androgen levels (up to adult values) show that ACTH is capable of causing adrenarchal changes in androgen secretion. Interestingly, after ACTH therapy there was no suppression of androgens below the pretreatment level in contrast to glucocorticoids. What causes adrenarche may not be a separate adrenal androgen stimulating hormone, but ACTH which gradually increases adrenal androgen secretion.

48

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Plasma cortisol and urinary melatonin in obese patients after a single dose of dexamethasone.

Previous studies have indicated that cortisol hypersecretion and abnormal cortisol responses to dexamethasone (DEX) could be both associated with low levels of plasma melatonin (MT). In this study, the possible relationship between urinary MT excretion (8 PM-8 AM) and the CRF-ACTH-Cortisol axis was investigated. 39 children and adolescents whose weight for age was above the 97th percentile received 2 mg of DEX at 8 PM. Plasma cortisol levels were determined at 8 AM and 5 PM before, and at 8 AM after DEX administration. 15 patients with a normal cortisol cycle (12.1 ± 1.4 and 3.1 ± 0.5 µg/100ml), and levels below 1.0 after DEX, showed a highly significant increase in MT excretion during the night following DEX administration (63.8 ± 5.6 ng/12h vs 33.1 ± 3.0 for the control night, $p<.001$). In a second group of 14 patients with mean cortisol levels similar at 8 AM and 5 PM (10.7 ± 1.3 and 9.3 ± 1.5), but with a normal cortisol decrease after DEX, nocturnal MT excretion increased from 21.5 ± 2.2 to 34.7 ± 5.6 ($p<0.02$). A third group of 10 patients with both poor cortisol cycles (16.1 ± 2.5 and 10.8 ± 2.4) and abnormal cortisol suppression after DEX (7.6 ± 2.1), showed no increase in MT excretion (24.2 ± 2.7 and 24.9 ± 3.7). The reciprocal changes in plasma cortisol and MT excretion in obese subjects suggest a relationship between the CRF-ACTH adrenal axis and the pineal gland.

49

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Measurement of plasma arginine vasopressin in the differential diagnosis of polyuria.

In children and adolescents (1-18 y, n:65) a linear correlation between plasma arginine vasopressin (AVP) and plasma osmolality (Posm), as well as between AVP and urine osmolality (Uosm) was observed. In polyuric patients AVP was measured following osmotic stimulation. After 12-16 h of water deprivation in control children AVP rose to 7.7 ± 3.2 pg/ml, Posm to 296 ± 9.0 and max. Uosm to 1024 ± 124 mosmol/kg ($\bar{x}\pm SD$, n:12). In patients with various tubular disorders impaired renal concentration was obtained (max. Uosm 370 ± 145, Posm 302 ± 11.6 mosmol/kg, n:7). AVP was higher as compared to the control group (14.0 ± 6.8 pg/ml). In 6 patients with central diabetes insipidus AVP was within the low normal range or below the detection limit of 0.8 pg/ml. By means of an infusion of hypertonic saline solution (5% NaCl, 0.04 ml/kg per min for 2 h) a partial defect in AVP release was separated from a complete one. Whereas in the complete form of central diabetes insipidus also at high Posm (>310 mosmol/kg) AVP was undetectable, it was measurable in the partial form, but inadequately low for concurrent Posm. Measurement of AVP during osmotic stimulation is of significance in the differential diagnosis of polyuria.

50

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Analysis of androgen-5&-reductase by an enzyme kinetic method.

Analysis of 5&-reductase(5&R) is commonly done by measurement of distinct testosterone(T) metabolites, following tissue incubation. Interlaboratory comparison is difficult, as different individual methods are used. In order to overcome this disadvantage, 5&R analysis was performed by evaluation of enzyme kinetics, according to Michaelis-Menten (Km- and Vmax-values), and by comparing the results with a conventional method. 17 tissue specimens (foreskin) of healthy boys (1 to 8 yrs) were examined with two methods (A and B). A: Conventional assay, using 8 pmol 3H-T as substrate. B: Evaluation of enzyme kinetics with increasing concentrations of 3H-T (8 to 208 pmol). Separation of metabolites by thin layer chromatography (TLC). Zone detection by computing radio TLC scanner. Control of purity and specific radioactivity by high resolution radio gas chromatography. Results showed age dependent values of 5&R ($\bar{x}$+SEM): Vmax=18.49+2.57 pmol/mg.h; Km= 102.82+11.41 nM, with a maximum at age 5 yrs: Vmax=36.33+4.32 pmol/mg.h; Km=171.77+23.53 nM.

Conclusion: It is recommended to evaluate 5&R-analysis by the enzyme kinetic method. The results of Vmax correspond to those obtained with the single point assay (method A, r=0.98). The advantage of method B is a reproduceable method giving biochemically absolute data for quality and quantitiy of the enzyme.

51

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Significance of steroid cell autoantibodies (SCA) in patients with APECED (autoimmune polyendocrinopathy - candidosis - ectodermal dystrophy).

Ovarian atrophy (OA), manifest as primary (PA) or secondary amenorrhea (SA) is common in APECED, being present in 64% of our postpubertal female patients. We determined in 26 female patients SCA, defined as reactive with ovarian, testicular and/or placental steroidogenic cells. SCA were found in 19 cases. 7 had PA, 6 had SA, 1 died accidentally before puberty, 1 remained prepubertal at 14.5 yrs and 4 menstruated normally. 1 of these 4 was infertile with irregular periods. The other 3 had normal periods; 2 have been pregnant (1 of them delivered a normal baby, the other chose abortion for social indications). All patients with SCA save 1 had primary adrenocortical failure (A). No patient with OA was negative for SCA (1-9 sera were studied per patient). It is unclear whether female APECED patients with SCA are bound to develop OA. Contrary to Elder et al (JCEM 1981:52:1137) it is also unclear whether patients with SCA are bound to have A.

Female APECED patients with SCA should be followed for development of OA and all patients with SCA for A. We have documented slow development of ovarian failure with serial GnRH test in 3 girls.

52

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Peripheral aromatase activity is a marker of androgen resistance in prepubertal children.

It has been suggested that rate of estrogen formation was higher in patients with Androgen Resistance Syndrome (ARS). This work was designed to find out if peripheral aromatase activity could be related to a defect in androgen action in prepubertal children with male pseudohermaphroditism. Fibroblast estrogen production was assayed by a highly specific enzymatic determination. Foreskin fibroblast strains were raised from 27 children with complete (C.ARS) or partial (P.ARS) androgen resistance as defined by dihydrotestosterone binding activity in cells. Results (mean ± SD) are expressed as pmoles estrone/mg proteins synthetized per day when cultured fibroblasts are incubated with Δ_4-androstenedione.

Normal (n = 17) = 7.8 ± 1.2
P.ARS (n = 23) = 18.3 ± 6
C.ARS (n = 4) = 24.2 ± 3
$p < 0.001$

These results show that -peripheral aromatase activity is low before puberty -fibroblast estrogen synthesis is significantly increased in prepubertal children with partial or complete ARS. Our data suggest that low utilization of androgens by target cells stimulates the production of estrogen. Peripheral aromatase activity can thus be considered as a marker of androgen resistance in prepubertal children with male pseudohermaphroditism.