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Familial X-linked Addison's disease (AD) without neurological symptoms as an expression of adrenoleukodystrophy (ALD).

Two brothers (pt.1 and 2) presented with hyperpigmentation at 5,and AD at 8yrs.Basal cortisol(F) was low or normal (102; 333),but did not respond to ACTH(113;336nmol/l).They were placed on substitution therapy and reevaluated at age 15 and 13 yrs. Puberty had developed in pt.1(P5,testicular volume 8ml), but not yet in pt.2.Both had no neurological symptoms. ACTH was increased(322;315ng/l),F low or normal(236;364),and DHA low(4.4;2.1nmol/l).Serum Ca,P,PTH,testosterone,and aldosterone,PRA,plasma and urinary adrenaline and noradrenaline before and after exercise,and LH and FSH before and after LHRH were normal in both.Antibodies against adrenal tissue were absent.A maternal uncle(pt.3) aged 35yrs also had hyperpigmentation since age 4,and AD since age 12yrs. without neurological symptoms,and was on long-standing substitution. Very long chain fatty acids(C24-26) were in the hemizygote range for ALD in the pts.,and in the heterozygote range in 3 asymptomatic obligate female carriers (mother of pts.1 and 2,daughters of pt. 3).This additional family with ALD without neurological manifestations suggests that all males with unexplained AD have to be investigated for ALD. Supported by the Swiss National Science Foundation (Grants No. 3.959-0.80 and 3.874-0.83).

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Measurement of plasma very long chain fatty acids (LCFA) in children with Addison's disease (AD).

Plasma LCFA were measured by gas-liquid chromatography in 2 groups of children aged 4 to 16 years with AD: group A: 13 boys diagnosed as adrenoleucodystrophy (ALD)on the basis of associated neurological symptoms and brain demyelination on the CT scan. Group B:12children, 9 boys and 3 girls without neurological symptoms and no evidence ALD. In group A, 10 boys had C24, C25, C26 levels and C24/C22 and C26/C22 ratios clearly in the ALD range. 2 were normal, as confirmed by measurements in skin fibroblast cultures. In group B, 12children had normal levels, but one boy had LCFA in the ALD range.

In conclusion LCFA measurement in children with AD lead to recognize ALD at an early stage in certain boys with apparently isolated AD, and demonstrated that the association AD-neurological disorders is not always synonym of ALD.

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The metyrapone test in pituitary dwarfs-determination of serum cortisol and 11-deoxycortisol by high performance liquid chromatography (HPLC)

Children with growth hormone deficiency may also have deficiencies of other pituitary hormones. The pituitary reserve of corticotropin (ACTH) may be evaluated in the metyrapone test. The purpose of the present study was to investigate the pituitary adrenal axis in a two day oral metyrapone test with simultaneous measurement of serum cortisol (F) and 11 deoxycortisol (S) level by HPLC in thirty children aged 5 - 16, with diagnosed growth hormone deficiency. Blood samples were collected before and after metyrapone administration. After metyrapone serum S levels over 8,7 µg/dl and F below 7 µg/dl excluded ACTH deficiency in 19 patients. Nine patients demostrated absent or subnormal ACTH reserve - fail to rise of S with F below 7 µg/dl. Two patients had no changes in serum levels of both S and F during the test, probably due to inadequate effect of metyrapone. To ensure that sufficient inhibition of cortisol production has occured, it is important to measure F in the serum as well as S. HPLC is therefore a very useful method of corticosteroid analysis especially for metyrapone test.

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Virilizing carcinoma of adrenal cortex in a female infant.

A girl aged 1.8 yrs presented with progressive facial acne, stage 3 pubic hair and clitoromegaly with no features of excess cortisol or oestradiol secretion. Growth was advanced; height +3.3 SD and bone age 3.4 yrs. Plasma and urinary androgens were:

Plasma (RIA)	Normal range	Basal	Post Dex. 2 mg daily x 2	Post-op.
DHEA-S (umol/l)	<0.5	1.45	1.45	<0.2
Δ4A (nmol/l)	<3.6	24.6	29.2	1.1
T (nmol/l)	<0.8	4.6	4.7	<0.5

Urine (GC)	Pre-op. (umol/24 hr)	Post-op. (umol/24 hr)
Androsterone	2.55	undetectable
Aetiocholanolone	3.88	undetectable
11β-hydroxy androsterone	2.20	undetectable
17-oxo steroids	9	<2

Abdominal ultrasound and CT scan showed a right adrenal mass. A 2 x 3 cm tumour was removed with no macroscopic signs of metastases. Histology showed mitoses and infiltration of adjacent cortex suggestive of malignancy. Five months post-op plasma and urinary androgens are normal. She is well with regression of clinical virilization.

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Endocrine complications of ACTH therapy of infantile spasms.

At the end of conventional ACTH therapy of infantile spasms sudden deteriorations of the infant's condition and even deaths are not rare. We followed 10 infants during and after carboxymethylcellulose ACTH therapy. 80 IU was given at 8 a.m. for 3 weeks and 40 IU for 2 weeks, with tapering during and termination at the end of the 6th week. During therapy 24h urinary cortisol increased 100-fold, morning plasma cortisol did not increase, and plasma aldosterone decreased slightly. After therapy, cortisol and AVP levels fell precipitously, cortisol remained subnormal for >2 weeks. Plasma renin and aldosterone peaked abruptly. Urine flow decreased and body weight increased sharply. Plasma cortisol response to AVP remained decreased for >2 weeks. Plasma cortisol response to ACTH was shortened at 3d and diminished at 1 to 2 weeks, indicating suppression of ACTH secretion. The risk at the end of ACTH therapy appears to be associated with 1) sudden subsidence of cortisol hypersecretion resulting in hypocortisolism and hypomineralocorticoidism 2) abrupt activation of the renin-angiotensin-aldosterone axis subsequent to the hypomineralocorticoidism, and 3) impairment of water excretion subsequent to the hypocortisolism.

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A case of Cushing disease treated successfully with bromocriptine:A paradoxical response to cyproheptadine

In a 11 4/12 years old girl Cushing disease due to pituitary adenoma was diagnosed and confirmed by CT examination.In order to select the pharmacological treatment prior to selective transphenoidal adenomectomy tests with single oral dose of bromocriptine, cyproheptadine and clonidine with RIA estimations of ACTH were performed. The following results were obtained (ACTH serum values in pg/ml):

0	30	60	90	120 min.	after oral dose of
10,0	71,0	285,0	86,5	55,1	cyproheptadine
60,8	15,1	20,6	26,7	37,5	clonidine
45,8	5,0	31,2	34,4	54,8	bromocriptine

The probatory treatment with clonidine was not effective. Three months after regular treatment with bromocriptine (7,5mg per day in 5 doses) a dramatic improvement was noticed. Serum cortisol level decreased and its rhythm became normal. A growth spurt, weight loss and lowering of the blood pressure were observed.When the patient was off treatment for 2 1/2 months, serum cortisol concentration increased especially in evening blood samples. She stopped growing, blood pressure increased and she put on weight again. After re-introducing the treatment remarkable improvement occured again.At the age of 12 she had menarche.After ten months of treatment the size of adenoma in CT image did not change, but its density markedly decreased; the patient is closely followed up.