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129 PROFILES OF STEROID EXCRETION IN THE NEONATAL PERIOD

Steroid excretion of infants with and without adrenal disease has been determined during the first weeks of life. Steroid conjugates were hydrolysed before conversion to thermostable derivatives for gas chromatographic (GC) analysis and combined GC-mass spectrometry. During the first days of life, steroid sulphates derived from the fetal adrenal zone predominate in all infants. These steroids were separated from the products of the definitive adrenal cortex which are excreted as free steroids and conjugates with glucuronic acid. Cortisol in the normal newborn is excreted as 1B and 6 hydroxylated metabolites. From studies of infants with adrenal hyperplasia cortisol biosynthetic precursors are metabolised differently in the neonatal period compared with their subsequent fate. Hence 17-hydroxy-progesterone is subject to active 15B-hydroxylation while 11-deoxycortisol is 6 -hydroxylated. These hydroxylation reactions are of minor importance after the first weeks of life. In premature infants the daily excretion rates of 5-ene steroids showed low amplitude oscillatory patterns with frequency like the pattern of maternal oestrogen excretion in the last trimester. No such pattern was observed from the excretion of cortisol metabolites. Thus, steroid reactions of the fetus are retained variably in neonatal life and the fate of steroids must be considered when evaluating the function and role of the adrenal at this time of life.

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132 Different ACTH response to i.v. metyrapon and hCRF in hypothalamic-pituitary hypofunction.

Previously we have demonstrated subnormal ACTH response with low basal ACTH level and normal basal cortisol level to i.v. metyrapon in hypothalamic-pituitary hypofunction (21st Ann.Meet.of ESPE, Helsinki,1982). The purpose of our present study was to asses the ACTH-cortisol responsiveness to CRF in the same patients. Human CRF (1-41) - hCRF (Bissendorf) - was given i.v. in the dose of 1 µg/kgbw at 8.00 a.m. after an overnight fast. Basal levels of ACTH (pg/ml) and cortisol (µg/100 ml) were measured before and 30, 60 and 90 minutes after hCRF application. In 5 patients with "ACTH-deficiency"(according to the i.v. metyrapon test) hCRF induced a detectable rise of ACTH, followed by an increase of cortisol secretion (Tabl.I). In 2 patients there were no significant changes of ACTH and cortisol levels.

Time:	0		30		60		90 min.	
	ACTH	cort.	ACTH	cort.	ACTH	cort.	ACTH	cort.
Mean:	13,7	12,3	54,3	21,9	30,6	22,7	18,8	19,7
SD:	10,4	5,9	6,4	8,5	11,6	6,1	13,8	4,2

The CRF test - similarly to GRF test for GH release - seems to be a much more effective method to study the ACTH release, than the metyrapon (or insulin) test(s).

130 ADRENAL INSUFFICIENCY IN INFANTS WITH NEONATAL ADRENOLEUKODYSTROPHY (NALD). P.Aubourg, P.F. Bougnères, F. Rocchicioli, J.L. Chaussain, Hôp. St Vincent de Paul, Paris.

We have developped a gas chromatographic-mass spectrometric method allowing the precise measurement of very long chain fatty acids (VLCFA) from microliter samples of plasma (J. Lip.Res., 1985,26). It allowed the early identification of 7 patients with NALD, who had a very distinctive pattern of plasma VLCFA when compared to controls as well as to children with childhood adrenoleukodystrophy (ALD):

VLCFA (ng/ml)	NALD (7)	ALD (7)	controls (40)
22:0	5936 ± 2416	22678 ± 6390	13011 ± 6450
24:0	9795 ± 4312	29502 ± 8434	10081 ± 5952
24:1	6821 ± 1836	13285 ± 4884	10132 ± 5557
26:0	2683 ± 1535	1088 ± 388	138 ± 74
26:1	1812 ± 588	258 ± 114	72 ± 42

In the absence of clinical signs, morning plasma cortisol was 6,9 ± 1,8 µg/dl (N=9,9 ± 2,9*),unresponsive to synacthen in the 2 patients tested, and ACTH was 121 ± 20 pg/ml (N< 90*). Although adrenal lesions have been described at autopsy in NALD,partial primary glucocorticoid deficiency was yet unrecognized, because of the absence of endocrine signs and uncertain identification of NALD before their early death. Thus NALD and ALD, two different diseases in terms of inheritance, neurological syndrome and VLCFA profiles nevertheless share the elevation of plasma C26 fatty acids and adrenal dysfunction.

* $p < 0,05$

133 URINE MASS SCREENING FOR NEUROBLASTOMA BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

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A mass screening program for neruoblastoma has been conducted since April 1984 in the Tokyo metropolitan area by means of HPLC. Dried urine spots on filter paper from infants aged 6 to 12 months were sent by mail to our laboratory. Urinary catecholamine metabolytes were extracted in ethylacetate using ten 5mm disks cut from the filter paper samples, and VMA, VLA and HVA were analyzed using HPLC (Shimadzu LC-4A) on reverse-phase ODS column by fluorometric detection. At the same time, the concentration of urine creatinine was measured by Jaffe's method using two 5mm disks. Positive correlation between urinary creatinine and/or VMA and HVA was found, however, the peak of VLA could not be found in normal infants. Since mean values of VMA and HVA in 141 urine samples from normal infants were 10 and 18.3 µg/mg creatinine, 20 and 35 µg/mg creatinine were chosen as the cut off points of VMA and HVA, respectively. Samples from 12484 infants were examined up until Dec. 1984, and 5 cases were recalled for re-examination. Finally 3 out of 5 cases were diagnosed as having neuroblastoma (two cases were stage I and one was stage III), and all cases were operated on successfully. In conclusion, the qualititative analysis of VMA and HVA of dried urine spots by HPLC is a recomendable method of mass-screening for neuroblastoma in the early stages.

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131 ANTIADRENAL AND ANTIPITUITARY CELLS ANTIBODIES IN CHILDREN WITH PRIMARY ADRENAL INSUFFICIENCY (PAI).

The detection of antiadrenal, antigonadotropic and corticotropic cells' antibodies by indirect immunofluorescence, was performed in 14 children with PAI : 4 with congenital adrenal hypoplasia (CAh) including 2 adolescents with documented LH deficiency, 6 with autoimmune syndrome and 4 with adrenoleucodystrophy. High titers of antiadrenal antibodies were found in the 6 patients with autoimmune associations while absent in the others. Anticorticotropic (8/14) and gonadotropic (10/14) cells antibodies were present in the 3 categories of patients, and antigonadotropic cells antibodies were constantly present at high titers in cases of CAh.

In conclusion 1) antiadrenal antibodies are specific of autoimmune PAI, 2) antipituitary immunity is frequent in children with PAI of various cases, 3) in patients with CAh, a relationship between high titers of antigonadotropic cells antibodies and the development of a LH deficiency can be discussed.

ASSESSMENT OF ADRENAL AUTOTRANSPLANTATION IN THE RAT BY WEIGHT GAIN AND STRESS RESPONSE. Andrew W. Saxe, Matthew H. Connors. University of California, Davis, Departments of Surgery and Pediatrics, Davis, CA USA.

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Because results of human adrenal autotransplants have been variable, we evaluated adrenal autotransplantation in rats. Female Sprague-Dawley rats were assigned to three groups: (1) bilateral adrenalectomy (ADx,n=8), (2) bilateral adrenalectomy with immediate autotransplantation of one-third of a gland to a flank muscle pocket (Tx,n=6) and (3) sham operation (S,n=6). The adrenal capsule was included with the transplant. Rats were randomly housed in pairs, provided saline and all survived the study. Adrenal function was assessed at 2, 4 and 6 weeks following surgery by measurement of corticosterone (C) 15 min after ether exposure to unconsciousness. Data from one animal in the Tx group was excluded because of finding residual adrenal tissue present in the retroperitoneum at autopsy. Weights of ADx animals were significantly below the other groups throughout the study ($p<.01$). The mean S group weight was not different from the Tx group after 2 weeks. Greater C concentrations were found in the S group at all study points. Mean C concentrations were not significantly different between ADx and Tx groups until 6 weeks. These observations indicate that in rats, one-third of an adrenal gland can be successfully autotransplanted to a muscle pocket. Graft function can be demonstrated at 2 weeks by comparison of body weight to ADx animals and at 6 weeks by comparison of C concentrations. This model can be used for studies with cryopreserved tissue along with radionuclide and NMR assessment of graft function.