5 H. FRISCH*, K. PARTH*, E. SCHOBER*, W. SWOBODA (Ped. Univ. Clinic and Boltzmann Inst., Vienna, Austria: Circadian levels of 17-OH progesterone (17-OHP), testosterone (T) and cortisol (F) in children with congenital adrenal hyperplasia (CAH) with and without treatment.

In 9 girls and 2 boys age 2 9/12 to 16 7/12 yrs. with CAH (21 hydroxylase deficiency) blood was drawn in 90 min intervals over a 24h period for determination of 17-OHP, T and F; 17 ketosteroids (17-KS) and pregnantriol (P_3) were measured in the 24h urine. These parameters were determined after interruption of therapy as well as under different therapeutic regimens. 17-OHP had marked diurnal variations; after treatment there was an inverse course of 17-OHP to the substituted corticosteroids; when the lower dose was given in the evening the onset of the nocturnal 17-OHP rise occured earlier and the levels were even higher; with all therapeutic regimens the T peak values were found during the night. The plasma F-levels distinctly reflected the orally administered dose of corticosteroids; in the untreated cases a decreased diurnal rhythm was observed. There was a good correlation between T and 17-KS as well as between 17-OHP and P_3, respectively. We conclude that: 1. the daytime of 17-OHP sampling and the interval to the drug administration should be standardized; 2. Corticosteroids should be administered 3 times daily with the highest dose in the evening.

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Saliva steroid measurement in childhood.

Saliva is an alternative fluid for steroid analyses in children. Sensitive RIAs have been developed for cortisol (F), 17OH-progesterone (17P) and progesterone (P) in parotid fluid and mixed saliva. Pre and post-TLC saliva values correlated for each steroid. A saliva F diurnal rhythm was seen in normals but not in Cushing's syndrome. Synacthen caused a rise in saliva F in normals but not in Addison's disease. CAH patients showed a correlation between plasma and saliva 17P levels (r=0.90). Saliva P levels increased on day 14 in 4 normal menstrual cycles, peaking 8 days later. Results indicate a practical role for saliva steroid measurements in paediatric endocrine disorders. Furthermore, the non-protein bound nature of steroids in saliva more accurately reflects plasma free steroid levels.

7 M. NEW, L. BRADLOW*, J. FISHMAN*, P. GUNCZLER*, G. ZANCONATO*, W. RAUH*, L. LEVINE*, S. ULICK*, Cornell Univ Med Col, Bronx VA, Rockefeller Univ, USA. Deficiency of Cortisol 11β-Ketoreductase — A New Metabolic Defect.

A deficiency of cortisol 11β-ketoreductase was observed in 2 patients with the syndrome of apparent mineralocorticoid excess and no evidence of oversecretion of any known steroid hormone. The syndrome is characterized by hypertension, hypokalemia and suppressed renin and ACTH despite low secretion of aldosterone, cortisol and other adrenocortical steroids. Excretion of 5α-reduced cortisol (DHF) is increased in the urinary free steroid fraction. The 11-ketoreductase deficiency was demonstrated by a markedly elevated ratio of urinary THF/THE (6-10). In normal children the THF/THE ratio is usually less than 1. The deficiency was further proven by demonstrating an inability to form tritiated water after infusion of $11\alpha^3H$ cortisol. In normal subjects and in the unaffected mother of a patient, 65-80% of $11\alpha^3H$ cortisol appeared as tritiated water. Speculation: In these patients the 11-ketoreductase deficiency produces an impairment of the metabolism of cortisol to cortisone, resulting in a prolonged cortisol half-life, suppression of ACTH and normal serum cortisol concentration. The enzyme defect protects the patient from adrenal insufficiency despite low cortisol secretion and may contribute to hypertension and hyporeninemia because of formation of excess DHF which has mineralocorticoid activity.

8 J. BLANKSTEIN*, C. FAIMAN*, F.I. REYES* and J.S.D. WINTER*(Intr. by C. Dacou-Voutetakis). Depts of Pediatrics, Obstetrics-Gynecology and Physiology, University of Manitoba, Winnipeg, Canada.

Partial 21-hydroxylase deficiency-A mild for of CAH?

Two sisters presented with hirsutism and anovular infertility. Both had female genitalia, normal puberty and normal BP. Urine 17KS were 20 mg, pregnanetriol 4 mg and cortisol 60 μg/24 hr. Serum testosterone (90 ng/dl) androstenedione (400 ng/dl), DHA (2000 ng/dl), progesterone (300 ng/dl), 17OH-progesterone (4000 ng/dl) and 21-desoxycortisol (1000 ng/dl) were increased. Serum cortisol, 11-desoxycortisol, DOC, corticosterone and aldosterone levels were normal. ACTH caused Na+ retention, hypokalemia and ↑ BP. Dexamethasone corrected the hormonal abnormality and was followed by ovulatory cycles. The data point to a partial 21-hydroxylase deficiency, presumably an autosomal recessive characteristic; two siblings are normal. Such partial defects may explain so-called late-onset CAH.

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Treatment of Cushing's Disease in Childhood by Transsphenoidal Resection of a Pituitary Microadenoma.

A 12 yr old girl presented with typical features of Cushing syndrome. Plasma F (17.8 μg/dl) showed a normal diurnal rhythm and dexamethasone (DX)-suppressibility. Urinary 17 KS (11.1 mg/24 h) and 17OH-C (20.1 mg/24 h) were increased but DX-suppressible, THE and THF showed a partial response to DX only. Free urinary F was 160 μg/m²/24 h (normal : < 50) and DX-suppressible. Plasma ACTH was 160 pg/ml (normal : <100). Treatment with aminoglutethimide (4 x 500 mg/day) for 8 months had a transitory effect only and cyproheptadine (16 mg/day) for 1 yr was unsuccessful. Plasma ACTH increased to 340 pg/ml. Sellar enlargement became evident. At transsphenoidal pituitary exploration a cystic microadenoma was resected. After surgery and pituitary irradiation transient ACTH deficiency was observed. Menstruation started 3 months postoperatively. T4 and T3 remained normal. The blunted TSH response to TRH was normalized. Responses of LH and FSH to LHRH, PRL to TRH and GH to arginine were normal.

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Neuropsychological study in treated thyroid dysgenesis.

60 patients aged 3-14 yrs, with hypothyroidism (HY) and athyreosis or ectopic thyroid gland, were examined for neuropsychological defects. They were selected on the basis of the following criteria: definite diagnosis of HY, absence of neonatal anoxia and of any factor predisposing to mental retardation, assessment of bone age (BA) at diagnosis, adequate therapy, normal subsequent physical development and hormonal control. The duration of HY was estimated as the time elapsed between BA at diagnosis and initiation of therapy. Psychoneurological defects were related to early HY according to the following schedule: Prenatal: hyperkinesis, short attention span, fine motor coordination disability; perinatal: impaired spatial orientation; 1-3 mo: slow ideation, enuresis; 2-4 mo: strabismus, articulatory speech defects; 2-12 mo: slow motor activity. In HY of prenatal onset, children treated before age 1 mo present some MBD symptoms which they compensate favourably with age; treatment after age 3 mo results in mental retardation, and after age 6 mo in cerebellar ataxy. HY starting at birth or later does not result in mental retardation.