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Growth Hormone and Adrenal Androgen Secretion

The effect of growth hormone (GH) on adrenal androgen secretion was assessed in 7 patients (5 males, 2 females) with GH deficiency but normal ACTH-cortisol function. Patients ranged in age from 9 3/12-14 8/12 years. Plasma concentrations of dehydroepiandrosterone (DHEA), its sulfate (DHEA-S) and androstenedione (Δ^4A), as well as urinary 17-ketosteroids and free cortisol were determined before, during short-term (2U/dx3) and after long-term (6 months) treatment with GH. The baseline, pretreatment plasma levels of DHEA-S were appropriate for the individuals' degree of skeletal maturation, whereas plasma DHEA and Δ^4A were undetectable (<42ng/dl and <27ng/dl, respectively) in 5/7 subjects. No significant change was noted in the plasma androgen values or in the urinary 17-ketosteroid and free cortisol concentrations during the short-term administration of GH. Despite a significant increase in growth velocity after 6 months of GH therapy, the pre- and post-treatment plasma and urinary steroid concentrations were not statistically different. These results fail to substantiate a role for GH in the secretion or metabolism of adrenal androgens. Thus, the delayed adrenarche and subnormal plasma adrenal androgen levels sometimes seen in GH deficient patients are not due to the absence of GH per se.

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Interactive effects of ACTH and growth hormone on adrenocortical hormone secretion.

The effects of ACTH and growth hormone (GH) on adrenocortical hormone secretion were studied in a 13-year-old girl with GH and thyrotropin deficiency but normal ACTH function. Cortisol secretion was measured by the sum of the urinary excretions of tetrahydrocortisol(THF), allotetrahydrocortisol(ATHF), and tetrahydrocortisone(THE). Adrenal androgen secretion was measured by the sum of androsterone(A) and etiocholanolone(E). The patient took a constant daily dose of desiccated thyroid(150mg) during 5 successive periods: 3-day control, 3 days of IM ACTH (0.5mg/kg daily), 12-day post-ACTH control, 6 days of IM human GH (3.5mg daily), and 3 days of ACTH + GH at the previous doses. Control excretion of THF + ATHF + THE was 6.0mg/g creatinine and of A+E was 2.9mg/g creatinine; these values confirm normal endogenous ACTH function. Taking these levels as 100, excretion of cortisol and androgen metabolites rose to 240 and 190 respectively during ACTH and decreased to 107 and 105 respectively during the last 3 days of the post-ACTH control period. During the GH period, they fell to 66 and 72 respectively. When ACTH was added to GH, they rose to 170 and 103 respectively. Thus GH given alone depressed secretion of both cortisol and adrenal androgens; this could be due to depression of endogenous ACTH secretion or to interference with the effect of ACTH on the adrenal. The data from the combined GH-ACTH period are compatible with either mechanism.

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Fluctuation of blood-spot 17-OH-progesterone level in infants with congenital adrenal hyperplasia.

Serial sampling for determination of 17-OH-progesterone by radioimmunoassay using dried capillary blood spots were performed throughout the day in eight infants with congenital adrenal hyperplasia due to 21-hydroxylase deficiency in order to check the value of a single random sample for identification of patients and in monitoring therapy. The samples were taken in different part of the country and sent into the laboratory by mail. Marked variation of dot-17-OHP values in a range of diagnostic high level was observed before starting therapy without any sign of diurnal rhythm. Repeated sampling for dot-17-OHP during the first weeks of glucocorticoid treatment showed persistent fluctuation at pathological high levels. While receiving glucocorticoid therapy for some months 17-OHP concentrations were suppressed showing moderately elevated levels in the morning and low levels in the evening. The blood-spot 17-OHP method can be used both for early identification and follow-up of congenital adrenal hyperplasia cases, however, 17-OHP profils over 24h are needed for monitoring therapy.

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17α-Hydroxylase-deficiency with unimpaired aldosterone formation in a male neonate.

Case report: This is the first report of a male neonate with 17α-hydroxylase deficiency with micropenis, hypospadia and normal aldosterone secretion. Diagnosis was based on elevated excretion of PD, DOC, TH-DOC, THB, allo-THB and decreased excretion of Cortisol, 11-desoxy-cortisol, THF, THE and testosterone. Serum levels of ACTH, LH, FSH, DOC were elevated whereas cortisol, testosterone and PRA were decreased. Serum levels and urinary excretion of aldosterone were normal.

Discussion: 17α-hydroxylase deficiency is a rare disorder of steroid metabolism. The clinical pattern in adults presents with hypokalaemic hypertension associated with metabolic alcalosis and pseudohermaphrodism in males. Low aldosterone levels indicate that the 17α-hydroxylase deficiency is linked to a dehydrogenase deficiency in the conversion of 18-OH-corticosterone to aldosterone. Our case presenting with unimpaired aldosterone formation may be a unique entity or due to unexpressed enzyme deficiency during the newborn period.

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17α-Hydroxylase and 5α-Reductase Deficiencies in a Newborn Male.

In a 46XY normotensive infant with micropenis, perineoscrotal hypospadias and a bifid scrotum with histologically normal testes, 17OH-deficiency was diagnosed from increased serum corticosterone (B) and progesterone (P) plus inadequate cortisol (F), testosterone (T) and DHA responses. Urine B metabolites were raised 100-fold; the 5α/5β-reduced metabolite ratio was normal before and after cortisol loading. Plasma Na, K, aldosterone and renin were normal.

	B (μg%)	P (ng%)	F (μg%)	T (ng%)	DHA (ng%)
Basal	22.0	475	8.8	25	<20
Post-hCG	16.0	-	-	59	<20
Post-ACTH	25.0	765	11.1	37	<20
Post-dexa	2.8	<35	4.5	<10	<20
Normal basal	<0.8	<100	20.0	20	90
Normal post-ACTH	3.4	177	65.0	20	150

Genital skin fibroblast T receptors were normal in vitro (23 fmol/mg) but surprisingly 5α-reductase activity was reduced (0.4 pM/μg DNA/hr), although Km for T (0.12 μM) and NADPH (170 μM) were normal. T therapy corrected the micropenis but not the 5α-reductase deficiency. Family study suggested reduced 17OH activity in the father and reduced 5α-reductase activity in the mother. Although the data suggest this boy may be a double heterozygote, a more direct link between 17OH-deficiency and target cell 5α-reductase cannot be excluded.

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17,20-Desmolase deficiency - clinical and biochemical heterogeneity.

3 XY-individuals were studied at a pubertal age. No. 1 and 2 were the original patients (Zachmann et al., Clin.Endocr. 1,369, 1972) with intersexuality, raised as boys. No. 3 (unrelated) had female external genitalia and was raised as girl. 1 and 2 had male puberty, but 3 not. Serum testosterone (T) before and after HCG (5000 IU/m2) was (ng/dl):

No.	age (y)	bone age (y)	basal	day 2	day 4	day 6
1	12.7	13.25	331	594	534	460
2	13.0	14.0	121	386	284	403
3	15.0	12.0	36	34	37	25

Androstenedione was low (62,76,29 ng/dl). 17OH-progesterone was normal or high (182,212,581 ng/dl) and increased after HCG (314, 381,1386 ng/dl), most in 3 with the lowest T. DHA before and after HCG was low in 1 and 2 (170-119,178-160 ng/dl), but normal in 3 (530-405 ng/dl). In urine, pregnanetriolone was present (0.62,0.32, 2.2mg/24h) and the 17-ketosteroids were normal or low (5.8,4.1,1.4 mg/24h). It is concluded that the degree of the defect may vary from partial (1 and 2) to marked (3) and that it may concern both, the Δ4- and Δ5-pathways (1 and 2), or the Δ4-pathway only (3).

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