111 CAH (21-HYDROXYLASE DEFICIENCY) PRESENTING AS CENTRAL PRECOCIOUS PUBERTY.

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A 14 year old female had the onset of pubic hair, breast development and mild acne at 6 to 7 years of age. The bone age was 3 1/2 years advanced. She had menarche at 9 years of age and has had monthly periods since. Early evaluation disclosed no abnormalities. The development of cystic acne at 10 years of age prompted additional evaluation. External genitalia were normal with no fusion of the labia and normal to small clitoris. There was no hirsutism. CT scan of the brain, ultrasound of pelvis, long bones, T_4,TSH, FSH (9.1 mIU/ml), LH (6.1),estradiol (51 and 148 pg/ml) were normal.DHEA-SO_4 (225 µg/dl). Elevated 17 OH-Progesterone (3028 ng/dl), androstenedione (350 ng/dl), testosterone (121 ng/dl) 24 hr urine 17 KS (14.9 mg),pregnanetriol (2.7 mg) normalized with Dexamethasone suppression and daily prednisone (5 mg) afterwards, to testosterone (34), 17 OH Progesterone (141 and 50), urinary 17 KS (5.3) and pregnanetriol (0.2). Serum 17 OH Progesterone in both parents and a brother were normal.

The findings are consistent with nonclassical CAH presenting with isosexual central precocious puberty probably as a result of increased biological maturity (as manifested by bone age) induced by CAH. CAH should be considered in the differential diagnosis of isosexual precocity in females.

Supported by John W. Champion

112 ACQUIRED PARTIAL 21-HYDROXYLASE DEFICIENCY IN A GIRL WITH PEUTZ-JEGHERS SYNDROME (PJS).

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A 12 yo gypsy girl with PJS s/p resection of adenocarcinoma of the colon at age 4 presented with hirsutism and menorrhagia of 9 months duration. Menarche occurred at age 10 initially with regular periods. Previous reports of an increased incidence of gonadal as well as GI neoplasms in PJS prompted a thorough investigation. Thyroid function was normal. A small left ovarian cyst was present by pelvic ultrasound. No ovarian/adrenal masses were present on abdominal CT scan. ACTH stimulation test (0.25 mg IM) and dexamethasone suppression test (0.5 mg po q 12h x 5d) showed:

		Cortisol µg/dl	17-OHP ng/ml	DHEA-S µg/ml	DHEA ng/ml	Δ_4A ng/ml	Δ5-17OHP ng/dl	T ng/dl
ACTH	0'	13	25	6.3	9	3.4	1240	35
	60'	24	74	4.6	17	8.6	1818	63
NORM	0'	10± 4	0.9±0.7	1.7±0.6	3.4±1.6	1.3±0.6	127±114	33±20
	60'	29± 5	3.3±1.9	1.9±0.7	10.5±3.8	2.4±1.1	985±327	41±21
DEX	pre	14	8	509	967	6.4	597	30
	post	0.6	0.38	170	78	3.6	30	10

The basal Δ5-17-OHP, 17-OHP, Δ_4A and DHEA-S were elevated. Low ratios of Δ5 17-OHP/17-OHP (0.5) and DHEA/Δ_4A (2.8) as well as high response of 17-OHP and Δ_4A to ACTH were diagnostic of partial 21 hydroxylase deficiency. Suppression of adrenal steroids by dexamethasone further supported this diagnosis.

113 11β-HYDROXYLASE DEFICIENCY-CONGENITAL DEFECT OR TUMOR.

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In 3 children with low renin hypertension and virilism, the hormonal profile distinguished the patient with an adrenal tumor producing DOC and androgens from the other 2 patients who had a genetic deficiency of steroid 11β-hydroxylase (11β-OHD). Clinical presentations were remarkably similar as were the baseline serum concentrations of deoxycorticosterone (DOC). The major difference in the baseline hormones consisted of very high DHEA levels in the tumor patient in contrast to very high androstenedione (Δ4) levels in the patients with the genetic defect of 11β-hydroxylation. The stimulation and suppression tests also distinguished the tumor patient. DOC did not stimulate with ACTH nor suppress with dexamethasone (dex). The PRA rose with dex suppression only in the patients with the genetic defect. Serum aldosterone was undetectable in all 3 patients in the baseline period.

	Age		Baseline			ACTH stimulation			Dex suppress		
			DOC	DHEA	Δ4	DOC	DHEA	Δ4	DOC	DHEA	Δ4
Pt	(yr)	Dx	(ng/dl)			(ng/dl)			(ng/dl)		
CH	2	tumor	243	708	47	248	875	51	287	871	82
FG	2	genetic	1746	267	818	14198	739	919	31	nd	65
DR	9	genetic	1039	436	1020	1834	491	981	nd	40	63

Conclusion: Though patients with adrenal tumors and those with a genetic deficiency of 11β-OHD have similar clinical presentations, similar PRA, aldosterone and DOC, the androgens and their steroid responses to ACTH and dex are clear distinguising features. (nd=not detectable)

114 RELATIONSHIP BETWEEN PLASMA-RENIN AND ACTH IN PATIENTS WITH CONGENITAL ADRENAL HYPERPLASIA

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Recent studies in patients with congenital adrenal hyperplasia (CAH) suggest that increased levels of plasma renin activity (PRA) and angiotensin II (AT II) during the salt-loosing state stimulate ACTH secretion (Rösler et al.). This study investigates the effects of different doses of the mineralocorticoid 9α- fluorohydrocortisone (9α -F) in CAH-patients with and without salt-wasting on PRA, AT II, ACTH, and adrenal steroids.

8 patients with CAH (aged 5 to 15 years : 5 girls, 3 boys, with (n=6) or without (n=2) salt wasting) were treated with both prednisolone (P) and 9α -F. PRA, AT II and ACTH were measured during 4 different periods of 2 days each with 1) P sine 9α -F, 2) P plus o.o5 mg 9α -F, 3) P plus o.1 mg 9α -F, 4) P plus o.2 mg 9α -F.

In 7 of the 8 patients a correlation between AT II and PRA activities and both ACTH and 17-OH-P levels was found. The study suggests: 1) PRA and/or AT II modulate ACTH secretion, 2) PRA levels may be influenced by 9α -F even in patients without salt wasting.

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M. GOURMELEN, B. GUEUX, M.T. PHAM-HUU-TRUNG, J. FIET, M.C. RAUX-DEMAY, F. GIRARD. Hop. Trousseau, Lab. explor. Fonction. endo. INSERM U 142 - Labo endo. Hop. St Louis, Paris, France.

Detection of heterozygous carrier for 21-hydroxylase deficiency by plasma 21-deoxycortisol measurement.

Plasma 21-deoxycortisol (21 DF) was measured by using an anti-serum raised in the rabbit with 21-deoxycortisol-3-O-carboxymethyl oxime-BSA. This anti-serum cross-reacted with 11-deoxycortisol (0.08%), corticosterone (0.35%), cortisol (0.6%) and 17-hydroxyprogesterone (1.6%). 21 DF was separated by celite partition chromatography and was eluted in the fraction isooctane 70v/ethylacetate 30v, together with 11-deoxycortisol and corticosterone. In 38 healthy volunteers (16 men and 22 women) 21 DF mean basal value was 166 pg/ml at 8 a.m. with a range of 66 - 401 pg/ml. After a Synacthen test, performed in 14 subjects, the maximum mean level was 414 pg/ml (151-930). In 31 congenital adrenal hyperplasia family members heterozygous for 21-hydroxylase deficiency proved by HLA genotyping, 21 DF mean basal level was 323 pg/ml (50-1,380). After Synacthen it increased up to 2,380 (1,070-9,060). In contrast with 17-hydroxyprogesterone which was also measured and which remained in the normal range after Synacthen in 12 cases out of the 31 , 21 DF under stimulation increased to pathological levels in all the cases studied. Therefore we believe that plasma 21 DF measurement could be of great interest in the biological detection of heterezygous subjects for 21-hydroxylase deficiency.

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DIAGNOSIS OF 17α-HYDROXYLASE-DEFICIENCY IN A NEWBORN FEMALE.

This is the first report of a female neonate with 17α-hydroxylase-deficiency. Very low oestrogen levels were observed in a 23 year old primigravida during an otherwise normal pregnancy. Normal excretion of steroid sulphates excluded placental sulphatase deficiency. A 2675 g female (46 XX) was delivered at term by induced labor. The baby was well and thrived with normal water and electrolyte balance. Since subnormal oestrogen levels during pregnancy may be due to failure of fetal steroid production, adrenal function studies were carried out. Unresponsiveness to ACTH was found at 6 and 13 days and 2 1/2 months of age. Androstenedione was subnormal. Urinary excretion of steroids were studies by TLC, HPLC and GLC at 13 days and 2 1/2 months of age. In the first sample 16-OH-pregnenolone and corticosterone were predominant steroids and the pattern was very similar to that described by Dean et al. in a newborn male with 17α-hydroxylase-deficiency. At 2 1/2 months of age the urinary steroid profile was similar to that found in adults with this deficiency.
We suggest that this infant whose Danish parents were unrelated with no relevant family history has a 17α-hydroxylase-deficiency. Treatment with cortisone lo mg per day was started at an early stage. Blood pressure and electrolytes are still normal and the child is now 6 months old.