123 LATE ONSET 21-OH-DEFICIENCY (21-OHD) CAN BE MISDIAGNOSED AS "TYPICAL PREMATURE PUBARCHE" (PP) IN CHILDHOOD.

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The isolated and early growth of pubic hair (PH) is often associated with slight advance in bone age (BA) and statural age (SA). Diagnosis of PP is classically made on high levels of dehydroepiandrosterone sulfate (DS). In this context, measuring only DS can be misleading, as we observed in 5 girls. The first 3 were seen at 5.5 yr for PP with normal SA ; their basal levels of DS (µg/dl) were indeed very high for age (135, 40 and 73 respectively). The last 2 girls were seen at 6-8 yr for early onset of PH (5-7 yr) and tall stature ; DS levels (63-94 and 86-158) were also very high. BA was advanced but not so drastically when reported to SA, except in girl n° 3. 21-OHD, suspected only in girl n° 5, was recognized in all girls on the systematic or retrospective (n° 1) measurement of 17-OH-progesterone (OHP) levels (ng/dl) which were variably elevated between girls (287 to 5372), but even more variable between days in each of them (ex: 87 to 2731 in n° 4). In girls n° 1, 3 and 4, OHP as well as DS were normally suppressed with Dexamethasone. Girl n° 1, misdiagnosed as PP until 16 yr, had normal menses from 12.7 yr onwards, still had high DS (362) and OHP (1246) levels at 18 yr but refused Rx. In girls n° 4 and 5, now treated for 2-3 yr, DS returned slowly to normal for age. In both girls, HLA-typing revealed the B14 antigen. In conclusion: 1) DS levels are high from a very young age in children with late onset or partial 21-OHD, in contrast to what observed in CAH newborns (Ped. Res., 1982, 16, 10) ; 2) Because 21-OHD can mimic the clinical and biological symptoms of "classical" PP, OHP should be measured systematically in children with PP.

124 PRENATAL DIAGNOSIS OF 17-KETOSTEROID REDUCTASE DEFICIENCY.

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In the index case, first child of the family, diagnosis of 17-ketosteroid reductase deficiency(17-KSRD) was made at 3 months of age on the response of testosterone(T) and Δ^4-androstenedone(Δ^4) after an hCG test : low levels (ng/dl) of T(101) but Δ^4 values (394) 10 times greater than the normal mean. At that time, the mother being pregnant again, requested a prenatal diagnosis. The proposed protocol included fetal karyotype, amniotic fluid (AF) steroid analysis at mid-pregnancy and ultrasound follow up of the genitalia. Prior to this study, AF levels of T,Δ^4 and individual Δ^4/T ratio were determined in 150 controls. In normal pregnancies AF Δ^4/T ratios are clearly ($p<0.01$) lower in male(4±1.6) than in female(12.8±4.5)fetuses. Based on the results (46,XY, AF levels low for T(5.9), high for Δ^4 (217) and extremely high Δ^4/T ratio (36.8), no phallic growth at ultrasound) the fetus was predicted affected. 17-KSRD was confirmed after birth : female phenotype, testes palpable in labia majora, typical response to hCG(T : 16→140; Δ^4: 48→601). At the mother's request the same protocol was used for prenatal diagnosis during the third pregnancy : karyotype was 46,XY but AF levels of T(14), Δ^4(57) and Δ^4/T ratio (4.2) were normal for a male fetus ; apparently normal genitalia were observed at ultrasound. The prediction was confirmed, since the boy was perfectly normal at birth. In conclusion. This study demonstrates for the first time the feasability of a prenatal diagnosis of 17-KSRD, as reported for an other testicular enzyme defect (17, 20-desmolase) (JCEM 1980,50,826).

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Plasma concentrations of androgens, cortisol and its precursors in virilizing adrenal tumors in children.

Five children (3 girls and 2 boys) aged 1 to 3 years were investigated. Virilization was isolated in 2 (group A), associated with Cushing's syndrome in 2 (group B) and with feminization in 1 (group C). The individual patterns of androgens were variable. However, in 4 out of 5 cases, the relative rises above normal levels (N) were greater for androstenedione (Δ_4) 4 to 100 times, than for dehydroepiandrosterone (DHA) 1.4 to 25 times. 11 β-OH-androstenedione (11 β-OH-Δ_4) measured in groups B and C, was found low normal in C (0.9 ng/ml) and high in B (2.8 and > 10 ng/ml) (N : 0.9 - 2 ng/ml). 17-OH-Progesterone was elevated in group B : 3.5 and 4.7 ng/ml and normal in groups B and C (N : 0.2 - 0.9 ng/ml). Only one of B patients showed a high cortisol level (255 ng/ml) 11-deoxycortisol levels were increased in all groups A, B and C.

Conclusions : a) androstenedione is the androgen the most prominently elevated

b) the rise in 11-déoxycortisol is a common feature

c) 11 β-OH-androstenedione may be low in spite of high levels of Δ_4

d) a possible mild block on 11 β-hydroxylation could be suspected in these tumors

126 GENERALIZED MINERALOCORTICOID UNRESPONSIVENESS : FAMILIAL RECESSIVE PSEUDOHYPOALDOSTERONISM.

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The present report describes two sibs - born from consanguineous Moroccan parents - presenting with severe salt wasting. Both had markedly elevated Na concentration in urine (84 & 63 mEq/L respectively), sweat (181 & 196), saliva (- & 120) and stool (- & 189), severe hyponatraemia (112 & 132) and hyperkaliaemia (10.7 & 7.3 mEq/L) in the presence of increased plasma aldosterone (PAldo > 8.5 & 5.4 ng/ml), plasma renin activity (PRA 40 & 18.9 ng AI/ml/hr) and urinary aldosterone (UAldo > 32 & 11.6 µg/day), indicating generalized unresponsiveness of aldosterone target organs. The parents investigated under basal and Na restricted diet appeared to be normal.

		PAldo	PRA	UAldo	Urine Na (mEq/day)	Sweat Na
Mother	basal	0.02	-	6.8	151	25
	restriction	0.40	2.0	49.6	11	-
Father	basal	0.03	0.9	8.5	101	37
	restriction	0.70	1.3	60.7	14	-
Controls	basal	< 0.21	<3.8	6-19	100-150	< 60
	restriction	-	-	18-85	< 25	-

Isolated renal unresponsiveness to mineralocorticoid hormones has been shown to be an autosomic dominant inherited disease. On the contrary, these results in two cases of generalized pseudohypoaldosteronism as well as the fact that two of the three yet published cases were born from consanguineous parents support an autosomic recessive mode of inheritance of the trait.

127 Abnormal Adrenal Steroids in Premature Virilization of Children.

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Adrenal steroids have been measured before and after acute IV ACTH stimulation (100 u Cortrosyn^R) in 25 prepubertally aged children with excessive virilization (pubic hair ± genital, somatic or skeletal growth excess).

Numbers of patients with basal levels <or> the upper limit of prepubertal values and > postpubertal values are:

	Prog	17 Prog	Cmpd S	DOC	Andro	DHA	DHAS
<Prepub-	14	15	14	8	5	4	5
>Prepub-	9	10	--	-	12	19	20
<Postpub-	2	--	5	3	--	2	--

Twelve had basal values in but not > the postpubertal range and normal incremental increases after ACTH and are considered to have premature adrenarche.

min	Prog ng/dl	17 Prog ng/dl	Cmpd S ng/dl	DOC ng/dl	Andro ng/dl	DHA ng/dl	DHAS µg/dl
0	29±17	61±28	99±34	11 ± 5	67±33	453±177	114±46
30	78±20	174±55	193±55	40±16	79±28	702±348	112±46

Among the other 13, 4 had basal levels > postpubertal, 5 excessive incremental response levels and 4 had both. Those in the latter 2 categories could be considered to have mild enzyme deficiencies, 2 with 11-hydroxylase, 3 with 21-hydroxylase, and 2 with 3-HSD. The children with the elevated basal levels without the expected rise after ACTH may represent abnormalities of enzyme regulation rather than enzyme deficiency.

128 INHERITED SUSCEPTIBILITY TO AUTOIMMUNE ADDISON'S DISEASE IS LINKED TO HLA-DR3 AND DR4.

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Inherited susceptibility to Addison's disease has been linked to the leukocyte antigen (HLA)-B8 allele, and by inference because of linkage disequilibrium between B8 and DR3, this susceptibility should be primarily to that of the DR3 antigen. Twenty four patients who had presented with overt Addison's disease, and another 28 patients who had been found to have adrenocortical autoantibodies, were HLA typed. Six of the Addisonian patients and 22 of the adrenal autoantibody positive patients had co-existing insulin dependent diabetes (IDD). In relation to HLA typing data from 253 Caucasian controls, Addison's disease was significantly associated with DR3 (χ^2 6.0 ; p = 0.014), DR4 (χ^2 7.4; p = 0.007) and DR3/DR4 heterozygosity (χ^2 25.4; p< 0.0001). Similiarly, adrenal autoantibodies in patients without Addison's disease (at the time of study) had increased frequencies of DR3 (χ^2 9.6; p = 0.003), DR4 (χ^2 12.6; p= 0.007) and DR3/DR4 (χ^2 15.2; p > 0.0001). Of the 6 Addison's patients who lacked DR3 and DR4 alleles in their HLA phenotype, 3 had type I autoimmune polyglandular syndrome.

In summary, these data indicate that susceptibility to autoimmune Addison's disease is associated with HLA-DR4 as well as DR3.