81 DEMONSTRATION OF MINERALOCORTICOID RECEPTOR DEFICIENCY IN TWO SIBLINGS WITH PSEUDOHYPOALDOSTEROENON(DH).
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Aldosterone(A) binding sites have been demonstrated in human membranes by an immunoprecipitation assay. The measurement of the mineralocorticoid binding capacity of these receptors could be a valuable tool to assess states of mineralocorticoid insensitivity in humans. In normal human plasma obtained at the time of surgery, the 8 y old girl was diagnosed in infancy after a severe salt-losing crisis. Plasma renin activity(PRA) and A were elevated. Treatment with hydrocortisone and dexamethasone lowered the plasma renin activity and hypertension. At this time PRA and A were normal but became elevated at 3 months of age. Both children received oral sodium supplementation. The plasma renin activity in the parents was within the normal adult range. These results are evidence that the A insensitivity in DH is due to a deficiency of mineralocorticoid receptors. It may be speculated that this deficiency is also present in other mineralocorticoid target organs in particular in the kidney. The existence of a small amount of receptor in the boy may explain the more favorable course in this child.

82 PRENATAL TREATMENT OF CONGENITAL ADRENAL HYPERPLASIA (CAH): FURTHER STUDIES IN MOTHERS AND CAH UNAFFECTED INFANTS. M. David*, N.G. Forrest* and H. Betuel*.
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In an attempt to prevent uterine visualization of female fetuses with CAH due to 21-hydroxylase deficiency, we have proposed the following protocol of treatment(Rx)(J. Ped 1984, 105, 799). This protocol is based on the suppression action of the adrenal androgens by dexamethasone(dex) given to the mother. Rx must be started before the critical time of sex differentiation (ie, before 5 wks). Dex was chosen because of its efficient placental transfer, lack of binding to plasma proteins and its prolonged half-life. The dosage of dex used (0.5 mg twice a day) was judged sufficient on biological parameters showing a suppression of maternal and fetal androgens. Diagnosis of CAH in utero was based on HLA typing of amniotic fluid cells in mid-pregnancy. Seven mothers at risk were started on such Rx at a mean of 7 wks' pregnancy. Except in one case (J. Ped 1984, 105, 799), the fetuses were found CAH unaffected. Rx was well tolerated in all mothers, but stopped at 20-22 wks when full prenatal diagnosis was achieved. Pregnancies were all uneventful and the 3 boys and the 3 girls were full term babies. These infants now aged 2-3 years had thus received a glucocorticoid and at somewhat physiological dosages during the first part of pregnancy also show normal developmental features.

83 MENDELIAN RATIO DISTURBION IN STEROLID 21-HYDOXYLASE DEFICIENCY (210D).
Steroid 210D is a monogenic, HLA-linked, recessively inherited condition. The homozygous affected state is not necessarily lethal. Penetrance is complete by criteria of ACTH-stimulated cortisol response. We report a distortion of the expected Mendelian ratio of 1 homozygous affected:2 heterozygous:1 homozygous unaffected amongst families studied with both ACTH-stimulated cortisol response and HLA typing. Specifically, we have observed a deficiency of heterozygous unaffected individuals. The mendelian ratio of 1:2:1 held true if HLA typing alone was considered. However, 50% of offspring predicted to be affected tested hormonally as heterozygotes, indicating that extremely rare, frequently, an unusual genotypic recombination had occurred. Neither parental gonadal or fetal gonadectomy nor haptotransmission distortion by specific HLA association. Using hormonal criteria alone, there was a 35% increase over the expected number of heterozygotes (p<0.005), resulting in a comparable decrease in homozygous unaffected individuals who had been ACTH-tested. Excluding one proband per family, there was no deviation from the expected proportion of homozygous affected individuals even when deceased sibs were included. Conclusion: In light of the excess number of heterozygotes, we feel that the genetic heterogeneity in 210D families, it appears that there is some pressure to transfert the haplotype segment bearing the gene for 210D. Whether this can be attributed to the 210D gene itself remains to be proven.

84 STUDY OF THE HUMAN GENE FOR THE CHOLESTEROL SIDE-CHAIN CLAVERING ENZYME, P450c20, (22 DESMIDELASE) IN CONGENITAL LIPOID ADRENAL HYPERPLASIA.
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Conversion of cholesterol to pregnalone is mediated by the single mitochondrial cholesterol side-chain cleaving (SCC) enzyme P450c20, formerly termed 22,20 desmolase. SCC activity in human congenital lipoid adrenal hyperplasia (Lipoid CAH) and direct evidence for absent P450c20 protein has been reported in one case. To determine if SCC deficiency is caused by absence of the gene, we obtained leukocytes from 3 of the 10 reported living patients with Lipoid CAH. Leukocyte DNA was cloned with restriction endonucleases and analyzed on Southern blots. Blots were probes with long chemically synthesized oligonucleotides containing 63 to 72 bases of the bovine P450c20 cDNA sequence, and with a 1 kb human P450c20 cDNA cloned in M13 libraries. Analysis of Northern blots of human and bovine adrenal mRNA indicate the P450c20 mRNA in 2.6 kb long and arises from promoter 46 kb long in both species. Indicating the P450c20 gene is about 6 kb. Analysis of Southern blots of DNA from the 3 patients and 8 controls showed no deletion in the human P450c20 gene, and no detectable restriction fragment length polymorphisms with the following enzymes: BamHI, EcoRI, HindIII, PstI, PvuII, and TaqI. We conclude that the absent SCC activity in the adrenal and gonadal patients with Lipoid CAH is not due to a large deletion in the P450c20 gene.

85 SIGNIFICANCE OF THE ADRENAL AND THE TESTES FOR THE PRODUCTION OF TESTOSTERONE (T) AND ANDROSTENEDIONE (AD) DURING MALE INFANCY. Frank B. Ingemier, Wolfgang Eisenhammer, Helmut W. Bircher, Gunter Ruhland, Children's Hospital and Institute for Forensic Pathology, University of Munich, Munich, FRG.

We previously reported high concentrations of T in infantile testes during the first 4 months of life and a sharp decline thereafter corresponding well to the plasma concentrations of T in this age group. In addition, A was lost as a non-correlate with plasma A concentrations. To study the significance of the adrenal cortex as another source of circulating corticoids in male infancy we measured T in whole adrenal glands of 28 boys, aged 0-2 years of age. The median concentrations found in different age groups are shown in the table (ng/ml).


3 Hirsute,unrelated girls(14,16,17,18yrs)with normal clitoral and regular(1) or irregular(2) menstruations were studied. Cortisol(c12.2-22.7 ug/dl),testosterone(68-107),17-OH-progesterone(595-1027),17-OH-progesterone(1074-2279) in normal and moderately increased, but DHEA(1023-1384ng/dl) was high. Also DHEAS (2730-6080 pg/ml) was high, indicating intact sulfon­dehydrogenase activity. In urine (captopril)300mg daily, more DHEAS was detectable after helicase, acid or glucuronidase hydrolysis,end low (0.4-3.0 mg/dl), or absent(2) after ACTH, but 16­hydroxylase was not detectable after ACTH. The DHEA and DHEAS were normal or slightly increased, and dehydroepiandrosterone-suppressible. When DHEA was added to urine, a peak appeared after helicase, excluding DHEA's sulfonation. Helicase inhibition CZE was in­jected 50mcg/(50mcg), DHEAS appeared in urine (0.9-2.9 mg/dl). With the same dose given to 2 normal girls (17-42 yrs), with normal basal plasma DHEA(85 and 95mcg/ml) more DHEAS (4.6-5.4 mg/dl), and also some 16OH-DHEAS appeared, unconjugated urinary DHEA in the pts. was similar as or higher than in normals. This new type of Hirsutism depends on DHEA threshold for DHEAS, but not for other steroids.Based on plasma steroid results alone, such pts.could be erroneously considered to have mild Conn's syndrome and should be considered different. Supported by Swiss National Science Foundation (Grant 3740883).