81 DEMONSTRATION OF MINERALOCORTICOID RECEPTOR DEFICIENCY IN TWO SIBLINGS WITH PSEUDOHYPOALDOSTERONISM(PH). Ursula Kuhnle, Helmuth Dörr, Thomas Strasser, Peter Weber, Dietrich Knorr, Decio Armanini. Children's Hospital and Internal Medicine Hospital, University of Munich, Munich, FRG.

Aldosterone(A) binding sites have been demonstrated in human mononuclear leucocytes(HML).The measurement of the mineralocorticoid binding capacity of these receptors could be a valuable tool to assess states of mineralocorticoid insensitivity in humans.

We here present data obtained in 2 sibs with PH and their parents. The 8 y old girl was diagnosed in infancy after a severe salt-losing crisis. Plsma renin activity(PRA) and A were elevated. In the 2 y old brother the diagnosis was suspected when hyponatraemia and hyperkalaemia occured in the first week of life. At this time PRA and A were normal but became elevated at 3months of age. Both children receive oral sodium supplementation, the dosage needed to normalize the sodium balance in the girl is considerably higher than in the younger brother. The parents show no signs of sodium imbalance.

When measuring the A binding in HML we found no binding sites in the girl. In the boy, there were 62 receptors/cell (r/c) as compared to 170±29 r/c in normal children. The binding sites in the parents were within the normal adult range. These results are strong evidence that the A insensivity in PH 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*, M.G. Forest*and H. Betuel*. Pediatric clinic, Inserm-U.34, Hôpital Debrousse and Centre de transfusion sanguine, Lyon, France.

In an attempt to prevent in utero virilization 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 suppressive action of the fetal adrenals by dexamethasone(dex) given to the mother. Rx must be started before the critical time of sex differenciation (ie. before9 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(.5 mg twice a day) was judged sufficient on biological parameters showing a suppression of maternal and fetal adrenals.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 uneventfull and the 3 boys and the 3 girls were fullterm babies. These infants now a few months to 3 year old having thus received a glucocorticoid'Rx at somewhat physiological dosages during the first part of pregnancy also show normal developmental features.

83 MENDELIAN RATIO DISTORTION IN STEROID 21-HYDROXYLASE DEFICIENCY (21OHD). P Speiser, MI New, New York Hosp-Cornell Med Ctr, Dept Ped, New York NY 10021

Steroid 21OHD is a monogenic, HLA-linked, recessively inherited condition. The homozygous affected state is not necessarily lethal. Penetrance is complete by criteria of ACTH-stimulated hormonal 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-stimulation and HLA-typing. Specifically, we have observed a paucity of homozygous unaffected individuals. The mendelian ratio of 1:2:1 held true if HLA typing alone was considered. However, 50% of offspring predicted by HLA type to be unaffected tested hormonally as heterozygotes, indicating that extremely frequent chromosomal recombination had occurred. Neither paternal nor maternal transmission distortion was observed; nor was haplotype transmission distorted by specific HLA associations. Using hormonal criteria solely, there was a 35% increase over the expected number of heterozygotes ($p < .005$), 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 and fewer than expected unaffected indi iduals among 21OHD families, it appears that there is some pressure to transmit the haplotype segment bearing the gene for 21OHD. Whether this can be attributed to the 21OHD gene itself remains to be proven.

84 STUDY OF THE HUMAN GENE FOR THE CHOLESTEROL SIDE-CHAIN CLEAVAGE ENZYME, P450scc (20,22 DESMOLASE) IN CONGENITAL LIPOID ADRENAL HYPERPLASIA. Karla J. Matteson, Bon-chu Chung, Walter L. Miller, University of California, San Francisco, Department of Pediatrics, San Francisco, CA, USA

Conversion of cholesterol to pregnenolone is mediated by the single mitochondrial cholesterol side-chain cleavage (SCC) enzyme P450scc, formerly termed 20,22 desmolase. SCC activity is absent in patients with congenital lipoid adrenal hyperplasia (lipoid CAH) and direct evidence for absent P450scc protein his been reported in one case. To determine if SCC deficiency is caused by deletion of the P450scc gene, we obtained leukocytes from 3 of the 10 reported living patients with lipoid CAH. Leukocyte DNA was cleaved with restriction endonucleases and analyzed on Southern blots. Blots were probed with long chemically synthesized oligonucleotides containing 63 to 72 bases of the bovine P450scc cDNA sequence, and with a 1 kb human P450scc cDNA cloned in our laboratory. Analysis of Northern blots of human and bovine adrenal mRNA indicate the P450scc mRNA is 2.0 kb long and arises from precursors ~6 kb long in both species, indicating the P450scc gene is about 6 kb. Analysis of Southern blots of DNA from the 3 patients and 8 controls showed no deletion in the human P450scc 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 adrenals and gonads of patients with lipoid CAH is not due to a large deletion in the P450scc gene.

85 SIGNIFICANCE OF THE ADRENALS AND THE TESTES FOR THE PRODUCTION OF TESTOSTERONE (T) AND ANDROSTENEDIONE (A) DURING MALE INFANCY. Frank Bidlingmaier, Wolfgang Eisenmenger, Helmuth Dörr, Ursula Kuhnle, Dietrich Knorr. 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. Testicular A was low and did not correlate with plasma A concentrations. To evaluate the significance of the adrenal cortex as another source of circulating androgens in male infancy we measured A and T in whole adrenals of 56 boys 1 day to 2 years of age. The median concentrations found in different age groups are shown in the table (ng/g adrenal tissue):

Month	1	2 - 3	4 - 6	7 - 12	12
A	186	37	17	10	10
T	21	5	3	2	2

The decrease of adrenal androgen concentrations during the first year of life parallels the involution of the adrenal fetal zone. There is a close correlation between the adrenal and the plasma concentrations of A but not of T. If we compare the total content of A and T in testes and adrenals we find at least 10 times more A in the adrenals than in the testes during the first 2 years of age. The testes contain more T than the adrenals only during the first 4 months. Thus we find that the adrenals are a major source of A during the first 2 years, after the 6th month of life they seem to be the main source even of T.

86 INCREASED PLASMA DHEA AND DHEAS AND ABSENT OR VERY LOW URINARY DHEAS, A NEW CAUSE OF HIRSUTISM (H). Milo Zachmann,Bianca Kempken,Brigitte Manella,Urs Eiholzer,Edmond A.Werder,Albert Otten,and Andrea Prader.U.of Zurich,Dept.Pediat.,Zurich;Kinderspital,Dept.Pediat.,St.Gallen,Switzerland,and U.of Giessen,Dept.Pediat.,Giessen,FRG.

3 Hirsute,unrelated girls(14.6-17.8yrs)with normal clitoris and regular(1) or irregular(2) menstruations were studied.Cortisol(12.2-22.7 ug/dl),testosterone(68-172),17α-OH-progesterone (107-479),and androstenedione(120-459ng/dl)in plasma were normal or moderately increased,but DHEA(1023-1384ng/dl) was high. Also DHEAS (2730-6080 ng/ml) was high,indicating intact sulfokinase. In urine (capillary column gas chromatography), DHEAS was undetectable after helicase, acid or glucuronidase hydrolysis,and low (0.4mg/d,1pt), or absent(2) after ACTH, but 16α OH-DHEAS was detectable before and after ACTH. Other conjugates were normal or slightly increased, and dexamethasone-suppressible.When DHEAS was added to urine, a peak appeared after helicase, excluding hydrolysis inhibition. When DHEAS was injected iv (50mg,2pts), DHEAS appeared in urine (0.9-2.9 mg/d). With the same dose given to 2 normal girls (17-18.4 yrs) with normal basal plasma DHEA(285 and 549ng/dl),more DHEAS (4.6-6.4 mg/d),and also some 16α-OH-DHEAS appeared.Unconjugated urinary DHEA in the pts.was similar as or higher than in the controls. This new type of H appears to be due to an increased renal threshold for DHEAS, but not for other steroids.Based on plasma steroid results alone, such pts.could be erroneously considered to have mild 3β-hydroxysteroid dehydrogenase deficiency. Supported by Swiss National Science Foundation (Grant 3874083)