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155 NO LINKAGE BETWEEN HLA AND COMBINED DEFICIENCY OF 21-HYDROXYLASE AND 17-20 DESMOLASE.

The conversion of the C21 steroids, 17-OH-Pregenolone and 17-OH-Progesterone (17-OH-P) to the C19 steroids DHEA: androstendione is mediated by the enzyme 17-20 desmolase. It was recently suggested that this enzyme deficiency is part of multiple abnormalities of steroid biosynthetic microsomal mixed function oxidases. We present a Jewish infant 46xy who was with micropallus at birth (1cm) with glandular hypospadias and normal testis. The child grew normally with normal blood pressure and no salt wasting Ultrasonography: mullerian duct derivatives absent. The child was raised as male. After treatment with HCG and testosterone (T) the penis size increased (4cm). Hormonal findings: basal levels of cortisol (F), high basal levels of progesterone (P) and 17-OH-P, and low basal levels of DHEA and T. P and 17-OH-P responded excessively to ACTH, while DHEA, T, desoxycorticosterone and F failed to rise, thus suggesting partial deficiency in both 17-20 desmolase as well as 21-hydroxylase. Both parents as well as two brothers did not have any signs of adrenal biosynthetic defect. HLA-typing revealed one HLA identical brother, thus suggesting that the gene for these enzyme deficiencies is not mapped to chromosome 6.

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156 THE VALUE OF CHORION VILLUS SAMPLING IN EARLY DETECTION OF 21 HYDROXYLASE DEFICIENCY (21-OHD).

Case history: The mother of a boy with classical 21-OHD was treated with Dexamethason (DXM) 2 x 0.5 mg per day during her second pregnancy. Therapy was started 5 wks after the last menstruation.Chorion villus sampling in the 9th week of gestation revealed the sex of the fetus to be female. The pattern of restriction fragment length polymorphism for the histocompatibility complex showed an identical A and B region in the chorion villus material both in the fetus and in the affected boy (A19.26;B27.40). DXM was continued until delivery. A non-virilised girl was born.
Salt loosing became apparent on the third day of life. Hormonal evaluation confirmed the diagnosis of classical 21-OHD (17α OH-Progesterone 580 nmol/l; Δ4A 38 nmol/l; T 6.5 nmol/l). Glucocorticoid and mineralocorticoid treatment was introduced.
Conclusion: DXM given during pregnancy prevented female pseudohermaphroditism in a girl with classical salt loosing 21-OHD. Chorion villus sampling is a useful technique to determine in an early stage of gestation, the HLA pattern of the fetus. This technique may be an adjunct in decisions as to whether to continue or discontinue the profylactic DXM therapy.

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157 PARTIAL INSENSITIVITY TO ANDROGENS IN SIBLINGS WITH DIFFERENT PHENOTYPIC ASPECTS : RECEPTORS-INDUCTION WITH LONG TERM ANDROGEN THERAPY.

Case 1 : Born 1976, female sex assigned, Karine. Examination at age 16 months : ambiguous genitalia (Prader II), phallus 1,5 cm length, with erections, palpable gonads in inguinal area ; genitography : rudimentary vagina. Laparotomy : no uterus, 2 testis with epididymis, normal histology. Caryotype XY. Testosterone raises from 14 to 208 ng% with HCG. At age 5, bilateral orchidectomy is performed and phalloplasty in order to suppress erections and to confirm female sex. At age 9, Karine is a well being little girl. Binding capacity of DHT receptors on sexual skin fibroblasts is 204 fentomoles/mg DNA, kd : 0,8 nM.
Case 2 : Born 1979, male sex assigned, Mickaël.Micropenis 0,5 cm length. No circonferential forehead skin. XY caryotype. Testosterone raises from 16 to 65 ng% with HCG. No mullerian structure seen at genitography. Normal male urethre. With androgen therapy, penis size reaches 4 cm length with erections and lack of bone age excess of maturation.
At age 6, orchidopexy. Fair male evolution. Before treatment, aged 2, binding capacity of DHT-receptors on sexual skin fibroblasts is 286 fentomoles/mg DNA, Kd : 0,65 nM (N : 400 to 800). At age 7, receptors level is 484 fentomoles/mg DNA, Kd : 0,33 nM on penis skin and 890 fentomoles/mg DNA, Kd : 0,54 nM on scrotal skin.
Then, a partial receptor deficiency is expressed in different phenotypic way in these two siblings with XY caryotype since the one was maintened in the female sex and the other in the male sex. In this latter, normalization of external genitalia was obtained with long term androgen therapy which is explained by the remarkable raise of receptor-sites observed at 5 years intervall.

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158 ANDROGEN INSENSITIVITY SYNDROME (AIS): CELLULAR RESPONSES TO ANDROGENS

A considerable number of hereditary defects in the mechanism of action of testosterone (T) is known. Most, but not all, can be traced back to either a functionally deficient receptor or a defect in the 5-alpha reductase activity. The current (in vitro) diagnostic approach involves cell culture of genital skin derived fibroblasts followed by studies of whole cell dihydrotestosterone (DHT) or R1881 uptake and the kinetics of T reduction.
Several receptor abnormalities can be detected only under special conditions: lability at 42°C; increased dissociation rate of the androgen receptor complex; different behaviour in the absence of molybdate, etc. A more or less complete investigation is therefore extremely time consuming, while in a significant percentage of all patients with the clinical diagnosis AIS, the diagnosis cannot be confirmed or excluded by means of laboratory studies. Therefore, we tried a functional approach: fibroblasts were stimulated for 6 days with T and DHT, followed by ^{35}S-methionine pulse-labeling. Labeled proteins were separated by means of 1- and 2-dimensional electrophoresis and detected by autoradiography. We found no evidence for the induction of new proteins, but the results suggest that under these conditions in normal androgen-responsive cells at least one protein disappears. In AIS patients no such repression was seen. This functional approach is able to corroborate and complement the "classical" receptor studies.

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159 INCOMPLETE TESTICULAR FEMINIZATION WITH INCOMPLETE MULLERIAN REGRESSION.

A 12 years old girl with clitoral hypertrophy, palpable testes in labia majora and prepubertal aspect of breast, pubic and axillary hair was evaluated. Her karyotype was 46 XY. Bone age was 9 years. Basal and peak FSH (34 and 104 mU/ml) and LH (10 and 49 mU/ml) were evaluated during a GnRH test. Testosterone levels (T), before and after HCG test (1000 U.I. every other day for 5 days), were 27 and 208 ng/dl, respectively; basal Estradiol, 17OHP and Cortisol during ACTH test and TSH, T3 and T4 during TRH test were in the normal range. Genitography revealed the presence of rudimentary uterus with a right tube. Histologic examination of removed testes showed bilaterally normal prepubertal testes. Neither ovarian nor dysplastic tissue was found. Two months after surgery, basal and peak FSH (37 and 103 mU/ml) and LH (11 and 62 mU/ml) levels persisted elevated during GnRH test; T (< 15 ng/dl) did not rise after HCG. This is the first report of incomplete testicular feminization with persistance of Mullerian structures probably due to a defective synthesis of MIF or some impairment of its action. Elevated FSH values, already reported in some cases of prepubertal TF, could be due to a decreased production of Inhibin.

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160 SEX HORMONE BINDING GLOBULIN RESPONSE TO THE ANABOLIC STEROID STANOZOLOL. PRELIMINARY EVIDENCE FOR IT'S SUITABILITY AS A BIOLOGICAL ANDROGEN SENSITIVITY TEST

Resistance to the action of androgens is the most common cause of male pseudohermaphroditism (PHM). Partial androgen resistance is characterized by varying degrees of ambiguous genitalia and the risk of virilization during puberty. The differentiation from other forms of PHM can be difficult. Attempts have been made to use biologic responses to exogenous testosterone as a test for androgen sensitivity, bearing the risk of undesired virilization of the phenotypically female infant. Androgens are known to suppress SHBG. Since in the testicular feminization syndrome not only the androgenic, but also the anabolic response is abolished, we investigated the effect of the anabolic steroid stanozolol on the SHBG-levels in plasma. Stanozolol was administered orally during 10 days (0.2 mg/kg up to max. 10 mg/dose) to 9 control subjects, 2 patients with complete and 3 patients with incomplete androgen insensivity. In the control subjects the SHBG-levels decreased dramatically irrespective of sex and age: 51.7% ± 3.5 (SD) of the initial values after 7 days, 39.6% after 10 days and 31.9% ± 7.0 (SD) after two weeks. In the patients with complete androgen insensivity the SHBG-levels remained unchanged, the moderate decrease in partial resistance was significantly different from the controls. Clinical effects or side effects of the stanozolol medication were not noted. We conclude that the detection of the SHBG-decrease following anabolic steroid administration seems to be a reliable, safe and simple test of androgen sensitivity.