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The pituitary-adrenal axis and the renin-angiotensin system in treated congenital adrenal hyperplasia.

41 out-patients, treated for 21-hydroxylase deficiency with oral cortisol (15 mg-30 mg/m^2), were studied at regular intervals. Among them were 24 salt-losers, who, in addition to cortisol, received 9 α-flurocortisol (20 µg-100 µg), and 17 non salt-losers. In the 1st group, plasma ACTH, 17OHP aldosterone and renin activity were (geometric mean) : 99.8 pg/ml, 28.8 ng/ml, 14.6 pg/ml and 8.4 ng/ml/h respectively. In the 2nd group, these values were 69 pg/ml, 57.9 ng/ml, 33.5 pg/ml and 2.3 ng/ml/h. There was no difference in ACTH mean levels, while 17OHP was significantly lower in the first group ($p < 0.05$). However, when choosing from the two groups the patients with similar 17OHP values, ACTH was found to be higher in the salt-losers, 126.9 pg/ml against 67 pg/ml in the non salt-losers ($p < 0.02$). These data suggest an inhibiting effect of angiotensin II (A II), at high concentrations, on the pattern of glucocorticoid synthesis, as has already been reported in man. Furthermore, we have noted that in isolated guinea pig adrenal cells, the cortisol output provoked by ACTH stimulation is decreased by the addition of A II.

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Endocrinology and cytology in juvenille goiter

We investigated 50 juvenile goiters between 6 and 17 years of age by means of total thyroxine (T_4), total triiodothyronine (T_3), thyroid binding index (TBI), thyrotropin (TSH) before and after 30min of TRH injection, thyroxine-binding globulin (TBG), thyroid antibodies and needle biopsies. 3 girls (6%) were found to have Hashimoto's thyroiditis. Antibody titers were positive in only one girl with associated Turner's syndrome and hyperthyroidism. Two additional girls had hyperthyroidism. Euthyroid children had mean T_4 of 8.85 µg/100 ml, T_3 1.72 ng/ml, TBG 23.7 µg/ml, TSH before and after TRH 3.18 µg and 17.38 µg/ml respectively. The incidence of Hashimoto's thyroiditis in juvenile goiter is lower than in the U.S.A. or Sweden probably due to the high incidence of iodine deficient goiters in this area of W-Germany.

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Serum Prolactin (Prl) in Normal and Delayed Male Puberty.

The function of Prl in the male is unknown. A relationship to adrenal androgens, esp. dehydroepiandrosterone sulfate (DS) has been suggested in hyperprolactinemic patients. We wondered whether the decreased DS concentrations noted in most boys with delayed puberty (DP) were associated with abnormal Prl secretion.
Serum Prl was determined after TRH(200 ug i.v.) in 10 normal (nl)boys, age 2-15y, Tanner(T) I-IV, and in 7 boys with DP, age 14-17y, T I-II. In addition Prl was measured 1/2hourly from 19^{00} to 7^{00} in 4 nl and 4 delayed prepubertal boys whose DS concentrations were similar.
Prl before and after TRH were not different in nl prepubertal and pubertal boys. Likewise basal and peak levels of Prl were similar in DP as in all nl boys (means 9.7 vs 10.9 and 35 vs 28 ng/ml NIH-VLS 1). During the night Prl was lower in the nl than the DP boys and showed less peaks. The means for the individual boys were 2.4, 4.5, 7.9, 9.1 (nl) vs 6.8, 15.1, 16.1, 17.0 ng/ml (DP).
Since TRH-induced Prl does not differ in normal and delayed puberty, and spontaneous secretion of Prl at night tends to be increased, low DS concentrations cannot be explained by a lack of Prl in delayed puberty.

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Serum dehydroepiandrosterone (DHA) and sulphate ($DHASO_4$) levels after acute growth hormone (hGH) therapy. An explanation for adrenarche?

The adrenal is a major source of increased levels of serum DHA and $DHASO_4$ seen in normal children approaching puberty. Factors controlling this "adrenarche" are little understood. Ten patients, 8 3/4 - 18½ years, 2F, 8M, 7 of whom had isolated hGH deficiency, were investigated. hGH (10 IU) was given intramuscularly on day 1; serum DHA and $DHASO_4$ were measured by RIA at 3, 6, 24 and 48h. A second dose of hGH (10 IU) was given and further samples taken at 3, 6 and 24h. Basal levels of DHA and $DHASO_4$ were consistent with pubertal status. Mean $DHASO_4$ levels fell significantly by 24 - 48h after the first dose, with variable rises in DHA. A DHA peak was noted 3h after the first injection in the mature patients. Mean $DHASO_4$ levels remained low after the 2nd dose, but DHA levels rose 24h later.

Conclusion: hGH may alter metabolism of $DHASO_4$ by increasing steroid sulphatase activity directly or indirectly which enhances conversion of $DHASO_4$ to DHA.

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Further studies on the developmental changes in adrenal secretion : pattern of the plasma levels of pregnenolone sulfate (PS).

PS is an adrenal steroid secreted in large amount as does dehydroepiandrosterone sulfate (DHAS). The aim of this work was to document if PS shows a different pattern with age as does DHAS and if their chronological changes are parallel. PS was measured in 300 normal subjects ; results are given in µg/dl ± SD. No sex difference was seen at any age. At birth cord levels (108 ± 50) and peripheral levels (87 ± 41), significantly different from each other, were the highest observed in life. PS decreased slowly then more rapidly from 1-6 months (25.8 ± 1.6) to 6-12 months (4 ± 2.7) respectively. Low levels (1.6 ± 0.9) seen at 1 to 9 yrs did not change until age 10, when PS increased progressively, but only 5 fold, until adulthood (7.8 ± 3.4). Thus 1) levels of PS are 10 to 14 higher in newborns than in adults while those of DHAS are similar ; 2) PS decreases less rapidly than DHAS during infancy. 3) PS does not rise abruptly as does DHAS at age 7 ; we conclude that PS is not involved in the secretory changes characteristic of the adrenarche.

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Androgen receptor levels in preputial skin from boys with hypospadias.

The level of high-affinity low capacity binding of [^{3}H] methyltrienolone ([^{3}H]MT) to human preputial skin cytosol in 7 boys with hypospadias and in 7 control subjects have been measured. [^{3}H]MT has been shown to have a specific affinity to the androgen receptor. The binding component was heat-labile, was totally destroyed by trypsin and the degradation at 0°C was slow (t 1/2=70 h). The time of dissociation of the ^{3}H MT-receptor complex at 0°C was slow (t 1/2=55 h). DHT and testosterone displaced [^{3}H] MT from the receptor whereas androstendione, progesterone, estradiol and R 5020 were much less effective competitors and cortisol did not compete. The dissociation constant of the ^{3}H MT-receptor complex varied between $0.17\text{-}2.17 \times 10^{-10}$M and the number of binding sites between 1.08-7.35 fmoles/mg protein. No significant differences were found between boys with hypospadias and control subjects. Procedure of collecting skin samples was approved by the Ethical Committee of Karolinska Sjukhuset.