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CONVENTIONAL STEROID THERAPY DOES NOT ADEQUATELY SUPPRESS 17OHP SECRETION IN CAH.

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Plasma 17OHP and cortisol levels were measured during continuous withdrawal (Cormed pump) at 30 min. intervals over 24 hrs in 9 patients (7F, 2M) aged 5½ to 18 yrs with congenital adrenal hyperplasia (21-OH def., CAH). Three patients were untreated (GR 1) and 6 were on hydrocortisone acetate (HC) 25-30 mg/m² with 50% of daily dose taken at 19-21 pm (GR 2). The mean plasma 17OHP level in the treated group was not adequately suppressed in the mid-night to 10 am samples although the 24hr mean was significantly lower in GR 2, mainly due to lower 17OHP levels in the 10 am to 11 pm period.

	Clock Time (hr)				17OHP (ng/dl, m±SD)	
	0 - 10	10 - 23	0 - 23			
GR 1	850 ± 856	450 ± 408	630 ± 739			
GR 2	748 ± 1115	257 ± 419	422 ± 938			
	p < .01		p < .01		p < .05	
	p < .01					

The 11OHCs levels in the treated group followed the normal circadian pattern, with sharp peaks of short duration due to HC intake. It is concluded that conventional HC therapy in CAH does not adequately suppress ACTH secretion throughout the day. It is suggested that 50% of the daily HC dose should be taken at 5-6 am instead of at night.

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GROWTH REDUCTION AND OBESITY, AN IRREVERSIBLE DAMAGE IN CHILDREN WITH CONGENITAL ADRENAL HYPERPLASIA (CAH) WHEN OVERTREATED WITH CORTICOSTEROIDS DURING INFANCY.

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In the literature, there are some reports stating that the quality of corticoid treatment in children with CAH does not have any effect on final height. This does not correspond with clinical experience in other forms of androgen excess. - 97 children with CAH were re-evaluated for corticoid treatment during their first 2 years of life. 36 of them had been overtreated with corticoid doses > 30 mg hydrocortisone equivalents/m²/day (mostly in the fifties and sixties). 61 had received adequate doses (< 30 mg/m²/day). 41 out of the 97 children had reached their final height. 17 of them belonged to the well-treated group; their mean final height was 1.6 cm less than the midparental height. 24 belonged to the overtreated group; their mean final height was 9.2 cm less than the midparental height (p<0.001). - In the overtreated group, the number of obese children (body weight >115% of ideal weight) was 27 out of 36, despite the fact that the hydrocortisone dosis had been reduced to about 20 mg/m²/day for many years. In the well-treated group, the number of obese children was only 7 out of 61 (p<0.0001). - Conclusion: For children with CAH, corticoid overtreatment in infancy is imprinting for life. If overtreatment occurs during the first 2 years of life, short stature and irreversible obesity cannot be avoided even if the dosis is corrected later on, and despite dietary restrictions.

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FETAL ADRENAL SIZE IS PITUITARY ACTH-DEPENDENT THROUGHOUT GESTATION.

Studies in a limited number of normal, anencephalic (Ac), and congenital adrenal hyperplasia (CAH) fetuses suggest that trophic factors other than ACTH may control adrenal growth in early fetal life. Combined adrenal weights were recorded in 102 fresh, non-macerated fetuses (gestational age, GA, 15-27 wk), 39 Ac fetuses (GA 13-25 wk) and 3 fetuses with CAH (GA, 17, 18.5, 30 wk). GA was calculated from the foot length. Mean adrenal weight in normals increased 4-fold between 15-27 wk. Adrenal weight did not increase in Ac fetuses between 13-21 wk. At 17 wk GA, mean ± SEM adrenal weights in normals (n=11) and Ac fetuses (n=8) were 1.0 ± 0.15 g and 0.3 ± 0.08 g respectively (p<0.001). Adrenal weights in 2 female CAH fetuses at this GA were 2.4 g and 4.4 g. Both had clitoromegaly and labial fusion; cardiac blood steroid levels in one fetus were: 17OH-progesterone 246, androstenedione 216, testosterone 22 nmol/L. A preterm (30 wk) CAH fetus who died also had large adrenals. Adrenal histology in all 3 CAH fetuses showed widening of the fetal zone and large cell size.

This comparative study of normal, Ac and CAH fetuses confirms the pivotal trophic role for ACTH in adrenal growth and steroidogenesis from early fetal life.

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EFFECTS OF TESTOSTERONE, EPIDERMAL GROWTH FACTOR (EGF), AND INSULIN ON RAT EPIDIDYMAL DIFFERENTIATION IN VITRO.

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Up to 14 days post natally, the rat epididymal epithelium is lined by undifferentiated cells. Thereafter several cell types start to differentiate among which the most common is the principal cell type with secretive and absorptive characteristics. Beside the testicular factors, the local factors of differentiation are poorly known. To provide new insights an *in vitro* culture system (Multiple Micro Chamber Module, Endotronics, USA) allowed the perfusion of fragments of epididymis of 14 days old rats, for 7 days in RPMI 1640 supplemented with penicillin and streptomycin at 37°C in 5% CO₂ 95% air. Thereafter the fragments were ultrastructurally analyzed. In this minimal medium, the epithelial cells showed no evidence of maturation and the peritubular cells largely increased their number. EGF (25 to 100 ng/ml) did not largely modified the epithelial cell maturation. Testosterone at 100 ng/ml or 1 µg/ml lead to principal cell differentiation with the appearance of apical microvilli, secretion vesicles and development of a supranuclear Golgi apparatus. The peritubular cells were well organized with numerous contacts with the epithelium. Insulin at 1 to 5 µg/ml had a similar effect on epididymal cells leading to a full differentiation of the principal cells contrasting with a poor organization of the peritubular cells. By place the basement membrane was thickened and most contacts between peritubular and epithelial cells were lost. As insulin was used in the range of "somatomedin C like" concentration, it is possible that the effect of testosterone on epithelial cells may be mediated by local secretion of somatomedin like factors. Other factors play on peritubular cells.

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DEVELOPMENTAL PATTERN OF PLASMA SEX STEROID BINDING PROTEIN (SBP) IN THE ANDROGEN INSENSITIVITY SYNDROME (AIS): PUBERTAL CHANGES INDEPENDENT OF SEX STEROIDS ? SBP was measured by a solid phase method in 80 plasma samples from 24 AIS subjects 1 mo-17 yr old. Results (µg/l) were compared to those found in 375 normal males matched for age. Weight was normal for height in all. In AIS infants, SBP was in the normal range. In AIS children, mean (±SD) SBP levels were 18.7±3.5 at 1-9 yr, and 14.4 ±5.3 at 11-13 yr, similar to that in normals (19.8±7.5 and 15.7±8.1). Values at 15-17 yr (13.1±5.6) were significantly (p<0.02) lower than at 1-9 yr, but higher than in normals matched for age (9.2±4.2) or testosterone (T) levels. A significant (p=0.03) correlation between SBP and age was found at 8-17 yr, but not before. These results are in general accordance with that of Cunningham et al. (JCEM, 1984, 58, 915) who reported a 38-46% fall in SBP in 2 AIS patients 8-16 yr old. The mean % fall is less in our larger series. In addition, we observed large individual variations, both in absolute values and in the degree of changes. This was even more evident in the longitudinal study made in 6 AIS patients: a significant correlation with age was found in only 3. In conclusion: 1) In AIS infants and children SBP is in the normal range. 2) After puberty, SBP is significantly higher in AIS than in normals. 3) At the normal age of puberty, mean SBP plasma levels fall of 30% in AIS patients versus 55% in controls; this difference may account for the influence of T in normal subjects. Assuming that in AIS, T is inactive on hepatic cell as in other target cells, then about half of the pubertal fall in SBP is not T-mediated.

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SEX STEROID BINDING PROTEIN (SBP) IN PREMATURE INFANTS We have recently reported that SBP is measurable in amniotic fluid: low levels with no sex difference, but showing a significant (p=0.02) correlation (r=0.587) with gestational age (GA). This prompted us to examine whether the postnatal pattern was different between premature and full-term infants. SBP was measured by a solid phase method in 102 plasma samples from healthy premature babies (28 to 38 weeks'GA) and in 290 samples from full-term infants matched for age (0 to 280 days). There was no sex difference at any age. Results from boys and girls were pooled and are given in µg/l of plasma. In the cord, a positive correlation between SBP and GA (r=0.42; p<0.01) was found. In peripheral blood, SBP was lower (p=0.02) in premature (4.9 ±1.9) than in full-term (7.1 ±3.3) infants 0-2 days old. A postnatal 3-4 fold rise was observed in both groups, with a significant correlation with age from day 0 to 30 (full-terms: r=0.723; n=120) (prematures: r=0.657; n=66). The rise lagged somewhat behind in prematures, whose levels were still significantly lower (9.8 ±4.9) than in full-terms (15.0 ±5.7) the 2nd week of life. Thereafter, SBP levels were not different in the successive age groups. In conclusion: 1) At birth, plasma SBP is lower in premature than in full-term infants. 2) A postnatal rise occurs in both, and by the third week of life values are similar. 3) Factors controlling the postnatal rise of SBP are poorly understood. Sex steroids do not play a role, since SBP rises dramatically at times when plasma estradiol drops and plasma testosterone rises in males infants. Whatever the factor(s) responsible, it is not related to prematurity.

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