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Assessment of gonadotrophin deficiency in pituitary dwarfism.

Fifty three patients with idiopathic (45) and organic (8) hypopituitarism, 43 boys and 10 girls, were studied during treatment with hGH. The gonadotrophin responses to GnRH (25 µg/m2) and serum levels of DHEA-s were measured yearly ; 15 patients remained prepubertal whereas 38 patients were studied before and during puberty occuring either spontaneously (11) or induced (27) by testosterone propionate (100 mg/mth) or ethinyloestradiol (10 µg/day)

Gonadarche and adrenarche were dissociated in some patients : among the 11 patients with spontaneous gonadarche, 2 had no previous biological adrenarche ; among the 27 gonadotrophin deficient (G.D.) patients, 9 had spontaneous adrenarche.

In prepubertal patients who were subsequently confirmed to be G.D., 27 GnRH tests were performed ; 23/27 integrated responses (I.R.) of FSH were found to be markedly lower than those observed in prepubertal controls of both sexes. In 9/27, I.R. of LH were below the control range. However, when in boys, I.R. of LH were analyzed according to bone age, 17/19 were below the lower limit of the control range.

These data might stress the importance of calculating I.R. of FSH to GnRH in hypopituitary patients in order to predict gonadotrophin deficiency.

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Postnatal changes in thyroid hormones and hormone-binding proteins in mother and infant with TBG deficiency.

Serial blood determinations of T4,T3,TSH,TBG,TBPA and albumin were made in a girl with partial TBG deficiency and her mother, who was suspected to suffer from hypothyroidism. In the girl normal se-TSH, low total se-T4 and se-T3 and a se-TBG level at 50% of normal for age and maturity were found at the 8th day of life. Se-TBPA and se-albumin value were normal. During a period of 22 months, the low se-TBG level remained unchanged; se-TBPA and albumin increased normally. Se-T3 but not se-T4 increased. In the mother the se-TBG level was (6 weeks after the delivery) similar to that of nonpregnant adults, but decreased gradually to a level, which was 50% of normal, indicating a TBG deficiency in the mother as well. A study of the family revealed 2 affected females with a se-TBG at about 50% and 3 affected males with a se-TBG at about 20% of normal level. An X-linked inheritance was suggested. The significance of the different postnatal pattern of TBG changes in mother and infant with partial TBG deficiency remains to be revealed.

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Response of adrenal steroids (AS), prolactin (PRL) and insulinlike-growth-factor I (IGF I) to high dose estrogens (HDE) in pubertal girls.

Dehydroepiandrosterone (DHEA), 17 OH-progesterone (17OHP), androstenedione (Δ_4A), testosterone (T), cortisol (F), PRL and IGF I were measured in plasma of pubertal girls (age 13,2±0,2 yrs) with tall stature before and on HDE. Results (mean + SEM (n):

days on HDE	0	25-50	50-100	
DHEA (ng/dl)	530±38 (37)	352±123 (23)**	271±90 (32)	* p<0,02
17 OHP (ng/dl)	168±50 (29)	87± 30 (22)***	104±16 (7)	** p<0,005
Δ_4A (ng/dl)	161±51 (32)	84± 6 (22)***	105±18 (9)	***p<0,001
T (ng/dl)	70± 8 (32)	56± 7 (22)	71±19 (6)	
F (µg/dl)	14± 1 (36)	14± 2 (23)	26± 6 (9)*	
IGF I (ng/ml)	260± 9 (12)	269± 31 (4)	269±13 (8)	50-200 days
PRL (ng/ml)	9± 1 (36)	30± 6 (18)***	19± 6 (6)	on HDE

All AS except F decreased. IGF I remained unchanged and PRL increased. The reducing effect of HDE on AS could be due to reduced production, increased metabolism and/or altered protein binding, but probably not to adrenal enzyme changes. F could remain normal or increase, because of increased transcortin. It is concluded that the reduction of adult height in HDE-treated girls is due neither to suppression of IGF I nor to stimulation of any of the measured adrenal androgens. Supported by the Swiss National Science Foundation (Grants No. 3.883.077 and 3.901.077).

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Reduction of the double stimuli hGH secretion tests.

In order to confirm the diagnosis of hormonal deficiency,upon inducing the secretion of GH by stimulation tests, dependable stimuli and more than one test must be employed.Numerous samples must be drawn with their consequent drawbacks.

A total of 79 patients (45 males, 34 females), 72 of whom suffering short stature and 7 obesity, underwent a double stimulation with L-Dopa plus Arginine (L-D+A) and Propranolol+Glucagon (P+G) following the methodology of Weldon et al. and Rochiccioli et al., respectively. The patient's ages ranged from 0 2/12 to 22 3/12 years old. There were no false negatives after P+G (0%) and 13.08% false negatives following L-D+A. After statistical analysis of the results, it was seen that the P+G stimulation test maintained its sensitivity upon reducing the number of samples used from 8 to only those drawn at 120' and 150' . The L-D+A stimulation test remained valide upon using only 4 (0', 20', 40' and 60') of the 7 proposed samples.

These results shorten the stimulation tests considerably.

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The age at menarche in ancient India as compared to the data from classical Greece and Rome.

In the industrially developed countries of the world the age at menarche had been getting 3-4 months earlier every decade for the last 100 years. Extrapolation backwards of this downward trend provides us with ridiculous figures. We, therefore, examined the recorded data from the writings of the authoritative Indian legislators during the period between ca.500 B.C. and 500 A.D. to study the trend in menarcheal age. Almost all of the legislators in their writings pointed out that the age of menarche was at 12 although full completion of puberty took place at age 16. The present day data differed from the ancient data being 0.8-1.2 yrs. and 2.2-2.4 yrs. later in the Urban and rural populations respectively. When the data from Classical Greece were examined from the writings of Aristotle and Hippocrates during 384-322 B.C. the age at menarche was between 13-14 yrs. The Roman authors Galen (129-199 A.D.),Soranus (2nd Century A.D.) found this age around 14, and Oribasius (4th Century A.D.) observed menarche to occur between 12-14 yrs. Thus the recorded data of the ancient time contrast with the current downward trend for the age at menarche.

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17-20 Desmolase deficiency in two unrelated prepubertal and adolescent boys previously diagnosed as simple hypospadias

In the 2 patients, 8 1/2 and 13yrs old, attention was drawn in the course of plastic surgery for perineoscrotal hypospadias by the small size of the phallus, the testis were palpable in the scrotum and there was a normal androgen sensitivity. In the older boy a small vaginal pouch was found; pubertal changes in hypothalamopituitary secretion were shown in the LHRH test (FSH:2,8-7; LH:5,6-60mIU/ml) and a large gynecomastia subsequently developped. Diagnosis of the enzyme defect was made by systematic endocrine studies in plasma (ng/dl) basal levels of testosterone (T), Androstenedione (A), DHA and DHAS were very low, while those of 17-OH progesterone (OHP) were very high (362 and 358). Dynamic studies were strikingly similar in both cases: no rise in plasma A and DHA after 250 µg/m2 of ACTH IV, an abnormally low rise in T (82 and 112) after HCG (7x1500 IU every other day) contrasting with an enormous rise in OHP after both ACTH (2330) and HCG (2757 and 964). Cortisol and aldosterone responses to ACTH were normal. In the urines (mg/day) the post ACTH rise in 17-OHSteroids were abnormally high (30.6 and 53.9) as compared with that of the ketogenic steroids (49.4 and 35.2). In the younger boy abnormally high levels of pregnanetriolone were found before (1.6) as well after ACTH (14.9). In conclusion, any child even with small ambiguity of his genitalia should benefit of detailed endocrine studies which may reveal that 17-20 Desmolase deficiency is not an exceptional disease.