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Plasma steroids in 3 beta-hydroxysteroid deshydrogenase (3 β OH-D) deficiency.

A 3 β OH-D deficiency was demonstrated in 4 boys with ambiguous genitalia and 1 girl with clitoromegaly aged 12 days to 4 years. Salt loss was overt in 3 cases, mild in 1, and in 1 was only detected by high plasma renin activity. Plasma dehydroepiandrosterone (DHA) was elevated according to age in all 5 patients (12 to 160 ng/ml), with an increased DHA/Δ 4 androstenedione (Δ 4 A) ratio, Δ4 A itself being slightly elevated in 3. All patients had increased plasma levels of 17 OH-progesterone (17 OH-P), 2.8 to 13.3 ng/ml, lower than in 21-hydroxylase deficiency.

These data demonstrate 1/ that measurement of plasma DHA and Δ4 A allows easy diagnosis of 3 β OH-D deficiency, with or without apparent salt loss ; 2/ that a limited increase of 17 OH-P, possibly related to an extra-adrenal 3 β OH-D activity, may paradoxically be an index leading to further diagnosis of 3 β OH-D deficiency based upon elevated DHA/Δ4 A ratio.

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Familial male pseudohermaphroditism due to 5α-reductase deficiency

Two Greek brothers (46XY) aged 16 and 18 years were brought up as females because of predominantly female external genitalia with clitoromegaly and urogenital sinus. At puberty there was genital masculinization with development of male musculature and body habitus without gynaecomastia. Both subjects changed from a female to a male gender role. Psychosexual orientation was male. Internal genitalia were normally formed with an ejaculate containing mature spermatozoa. In both subjects plasma testosterone(T) and androstenedione(A) were elevated, dihydrotestosterone(DHT) was in the low normal range and the plasma T/DHT ratio was elevated (34, 36). Plasma oestrogens were normal whereas SHBG binding capacity was elevated. The urinary 5β-aetiocholanolone/5α-androsterone ratios were elevated compared with normal subjects. Basal LH was normal but the LH response to LH-RH was exaggerated. Basal and peak FSH were elevated. The clinical and hormonal features are consistent with impaired peripheral conversion of T to DHT due to deficiency of 5α-reductase.

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17-Ketosteroid Reductase Deficiency - Plasma Steroids and Incubation Studies with Testicular Tissue.

In infancy, the proposita was diagnosed as a case of testicular feminisation. At the age of 14 she suffered from severe symptoms of virilising puberty with poor breast development. Plasma steroid analyses revealed a tenfold elevated androstenedione concentration (Δ4 = 1562 ng/dl). Testosterone (T = 266 ng/dl) was in the pubertal range. Thus the Δ4/T-ratio was far above normal. The estrone/estradiol ratio was also elevated (E1/E2 = 10.2/2.2 ng/dl). Δ4, T, E1, and E2 could not be suppressed by dexamethasone, but reacted promptly to fluoxymesterone (Δ4 =781 ng/dl). HCG caused a further increase of the Δ4/T-ratio(2220/246 ng/dl); ACTH did not alter the Δ4-concentration. These findings together with similar investigations after gonadectomy suggest that the failure to convert Δ4 to T and E1 to E2 is restricted to the testes. In-vitro incubations of testicular tissue showed almost no 17-ketosteroid reductase activity.

This form of male pseudohermaphroditism can easily be detected already in infancy, if steroid analyses and stimulation tests are performed, and patients should be submitted to early orchidectomy in order to avoid virilisation in puberty.

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Oxandrolone treatment for growth promotion in Turner's syndrome.

Progressive growth failure in patients with the pure form or mosaicism of Turner's syndrome causes short stature. Oxandrolone (Ox) has been reported as being effective in producing acceleration in height in these patients. 25 patients 10 to 17 years old were treated orally with Ox in a dosage of 0.1 mg/kg/day for 1 to 3.5 years. Growth velocity per year (mean ± SD) for all patients was 2.8 ± 1.0 cm before treatment and 5.3 ± 2.1, 3.9 ± 1.9 and 2.8 ± 1.8 cm after 1,2 and 3 years of therapy, respectively. Patients younger than 14 years exhibited the best response. Bone age remained retarded during treatment. Using the method of Bayley and Pinneau for height prediction we found that the estimated height increased from 143.2 ± 5.4 to 145.8 ± 5.9 cm for all patients after 1 year of treatment. A 3 year follow-up of 8 patients showed an increase of predicted height from 140.6 ± 5.1 cm to 146.1 ± 4.6 cm. Our data indicate that Ox has a beneficial effect ($p < 0.001$) on growth velocity for the first year of therapy and may cause a moderate gain in final adult height.

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Effects of Oxandrolone on Growth in Turner's Syndrome.

16 patients with XO-syndrome, aged 11.1 - 16.3 years, were treated with 0.1 mg/kg oxandrolone daily. Mean bone age 11.3 ± 1.1 (SD) years, height SDS (standard deviation score) for chronological age 3.45 ± 0.94.

Pat. received oxandrolone therapy for one year (p e r i o d I), no therapy for the next 6 months (p e r i o d II) and oxandrolone again for further six-month periods (p e r i o d III, IV).

There was a significant increase ($p < 0.005$) in growth velocity (cm/year) with hormone medication: pretreatment: 2.3 ± 1.2, during first and second 6 months of therapy: 5.9 ± 1.6 and 5.2 ± 0.9, during period II: 1.4 ± 1.1, period III: 4.6 ± 1.4, period IV: 4.0 ± 0.5. Bone age velocity did not differ significantly from pretreatment velocity during period I-IV. Oxandrolone treatment resulted in a significant increase ($p < 0.005$) in the ratio of height age: bone age. Height SDS for bone age significantly decreased ($p < 0.01$) with hormone administration: pretreatment: -1.72 ± 0.76, after period I: -1.41 ± 0.76, after period II: -1.69 ± 0.75, after period III: -1.49 ± 0.66 and after period IV: -1.51 ± 0.62. Serious side-effects were not observed.

These data may suggest some favourable effect of oxandrolone on growth in Turner's syndrome.

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Studies in clomiphene (C) treated pubertal boys with gynecomastia (G).

Plasma LH and FSH, basal (b) and after LHRH (p), testosterone (T), estradiol (E_2), estrone (E_1), androstenedione (Δ_4A) and prolactin (PRL) were determined in 5 pubertal boys with G before, during and after 50 mg C daily for 56 days (d). Results (mean, SEM):

	pre-treatment	on treatment 14d	on treatment 56d	posttreatment 18d	posttreatment 61d
LHb	22±3	41±16	54±27	25±5	22±5
LHp (ng/ml)	110±31	140±43	169±60	151±63	76±10
FSHb LER 907	82±29	200±99	220±106	80±29	39±14
FSHp	187±59	252±102	358±173	205±102	97±23
PRL(ng/ml,n=4)	9±1	7±1	6±2	7±1	6±1
T(ng/dl)	361±88	818±95	1009±144	489±119	430±119
E_2(pg/ml)	47±10	66±9	82±8	38±3	30±4
E_1(pg/ml)	110±8	162±26	177±20	107±17	119±20
Δ_4A(ng/dl)	215±85	261±83	255±57	155±13	150±26

In conclusion, C increases gonadotropins and testicular steroids. In spite of higher E_1 and E_2, G is reduced in most patients. This may be due to a higher T/E_2 ratio or interference of C with E_2 at the receptor site.

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