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Prostatic concentrations of androgens and androgen-receptors in developing rats.

Testosterone (T), 5 α -dihydrotestosterone (DHT), 3 α ,5 α -androstenediol, and DHT-receptors (DHT-R) were measured systematically in the prostatic cytosol of developing rats from age day 20 (immature) through age day 56 (spermatogenesis complete). The profiles obtained at various maturational stages demonstrate that the prostatic contents of androgens and DHT-receptors are high in the immature animals (T 0.203 ng/mg DNA, DHT-R 1.700 fmol/mg prostate), fall drastically just before the onset of puberty (T 0.058, DHT-R 0.533), then peak sharply at age day 35 (T 0.739, DHT-R 1.830), and slowly tail off with increasing age (day 45: T 0.232, DHT-R 0.733) and by age day 56 although T remains low (0.116) DHT-R has a second peak (1.28). The profiles of the prostatic contents of androgens and androgen-receptors demonstrate a divergence from the pattern of circulating T, DHT and LH during sexual maturation, but somehow parallels the pattern of circulating FSH till day 50. It is possible that FSH plays an important role in the regulation of intraprostatic androgens and androgen-receptors during sexual maturation.

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Sexual Development in Apparently Nonmosaic Turner's Syndrome (XO).

Two girls with many features of Turner's syndrome and XO karyotypes menstruate regularly at ages 14 and 15. Menarches occurred at 10 yrs 11 mos and 13 yrs 5 mos. Laparoscopy in patient 1 showed grossly normal ovaries. Biopsies (40 mm³ on right and 24 mm³ on left) showed stroma with no follicles in the right and stroma with 1 atretic and one primordial follicle in the left ovary. Patient 2 had a cystic 2x2-cm. left and a yellow-white streak right ovary with a 1-cm. paraovarian cyst. 2-mm³ biopsy of the right ovary showed an atretic follicle. 72-mm³ biopsy of the left ovary yielded 8 or fewer primordial and atretic follicles and part of one Graafian follicle. LH and FSH during follicular phase were 11.1 and 15.8 mIU/ml in pt. 1 and 4.5 and 12.4 mIU/ml in pt. 2. Total serum estrogens in pt. 1 were 137 pg/ml. Studies of responses to LHRH are in progress. Buccal smears from the girls showed Barr bodies in 1/200 and 0/200 cells respectively. Karyotypes of three separate blood lymphocyte preparations and one ovarian fibroblast preparation from pt. 1 and one blood lymphocyte preparation from pt. 2 show only 45X with no evidence of mosaicism. Further chromosome studies are in progress.

Traditionally, sexual development in 45X patients is attributed to occult mosaicism. Since both X's are active in the ovary before meiotic entry, we believe the 45X complement just accelerates the normal atresia of oocytes and that these girls are not mosaics.

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Diagnosis of hypogonadotrophism versus delayed puberty in the male at pubertal age.

This differentiation often appears impossible at pubertal age. In groups of boys the conditions differ in plasma testosterone response to HCG and LH response to GnRH. However, in clinically unclear individual cases the tests often fail too. We have followed 32 boys until the diagnosis of hypogonadotrophism was clinically certain. All had been given a GnRH test (3.5 μ g/kg up to the maximum of 100 μ g GnRH iv) and some an HCG test (5000 IU/m² im on days 1, 3, 8 and 10, with determination of serum testosterone on days 1 and 15). We have compared their results with the results of 68 normal boys at similar, usually markedly delayed development. Every primary test parameter showed an overlap between the two groups. Best in discrimination were the logarithms of stimulated testosterone level (lnTs) and maximal increment in LH level (ln Δ LHmax). The lower limit of 90% confidence range for lnTs in the reference series detected 6/8 of the hypogonadotrophic against none of the reference boys. The same limit for ln Δ LHmax detected 64% of the hypogonadotrophic boys in 47 tests against 4% of the reference boys. The product of these two parameters (lnTs x ln Δ LHmax) appears superior. Data being so far available for 8 hypogonadotrophic and 17 reference boys, these groups are completely separated by the product, and with a wide margin. Further data are being collected to allow a reliable evaluation of this new diagnostic parameter.

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Plasma steroid levels in thalassemic girls, University of Cagliari, Italy.

Thalassemia Major, a severe disease principally characterized by chronic hemolytic anemia is frequently associated with delayed sexual maturation. 12 thalassemic girls aged from 18 to 22 years at Tanner's first stage of puberty and 12 healthy girls at the same age but at the fifth stage of puberty, were studied. After informed consent of parents, blood samples were taken at 8-9 a.m., after overnight fasting. Specific RIA was measured FSH, LH, Prolactin (PrL), Cortisol (F) and Dehydroepiandrosterone sulphate (DHA-S) directly in the plasma. Plasma ether extraction and celite column chromatography were performed to measure by RIA the following hormones: Dehydroepiandrosterone (DHA), Pregnenolone (Δ 5P), Progesterone (P), 17OHPregesterone (17P), Androstenedione (A), Testosterone (T), Dihydrotestosterone (DHT) and Estradiol (E2). Results from healthy to thalassemic girls: FSH (from 9 to 4 mIU/ml), LH (from 9 to 2.5 mIU/ml), PrL (from 10 to 6 ng/ml), F (from 120 to 80 ng/ml), DHA-S (from 1.8 to 0.08 μ g/ml), Δ 5P (from 1.6 to 0.5 ng/ml), P (from 270 to 110 ng/ml), 17P (from 0.43 to 0.15 ng/ml), A (from 10 to 2.5 ng/ml), T (from 0.4 to 0.1 ng/ml), DHT (from 120 to 25 pg/ml) and E2 (from 85 to 50 pg/ml). These data suggest that thalassemic girls show a delayed adrenarche, according to our previous studies due to the abnormal iron deposits.

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Pubic hair in boys due to adrenarche rather than true puberty.

Pubic hair sometimes develops in boys before testicular enlargement. We have tested the possibility that this situation can be due to adrenarche rather than true puberty.

Eight cases between 5.5 and 12.8 years of age were observed to have stage III pubic hair and prepubertal-size testes. All were healthy; 5 were obese. Plasma dehydroepiandrosterone sulphate (DHA-S) levels were 94-228 μ g/dl, above the 95% limits for age. Plasma testosterone at 0800-1300 hr was 11-28 ng/dl. Bone age was normal or only slightly advanced.

Diurnal blood sampling and ACTH testing were carried out in an 8.6 year old case. Daytime and nighttime testosterone were similar (16-30 ng/dl), ruling out early true sexual precocity. His baseline pattern and response of steroid intermediates to ACTH was typical of premature adrenarche, ruling out adrenogenital syndrome. In two other cases the pattern of plasma steroid intermediates was normal and DHA-S was shown to be normally dexamethasone-suppressible.

These studies show that isolated onset of pubic hair in boys without testicular enlargement does not necessarily indicate true puberty or virilization, but is often due to adrenarche as a variation of normal. Furthermore, these results suggest an association between premature adrenarche and obesity.

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Testicular dysfunction after combination chemotherapy for Hodgkin's disease in childhood.

Testicular function was studied in 15 males, previously treated with combination CT (mustine, vincristine, procarbazine and prednisolone) for Hodgkin's disease in childhood. All were investigated (at least once) between 1 and 8 years after the end of CT. The 3 boys, who were still prepubertal, showed normal basal FSH and LH levels and gonadotrophin responses to LHRH. Three of the 5 studied in early puberty and 8 out of 10 in late puberty or adulthood showed a raised basal FSH level and an exaggerated FSH response to LHRH. Seven of the 11, with an elevated FSH level, showed similar abnormalities of LH secretion. Basal testosterone levels were appropriate for pubertal status in all patients but a few showed an impaired testosterone response to HCG stimulation. Nine of the 10 late pubertal or adult males had small testes and, in 6 cases, azoospermia. In conclusion combination CT (MVPP) in childhood appears to cause severe and probably irreversible damage to the tubular system of the testis. Subtle biochemical evidence of Leydig cell impairment may be present but clinical features of androgen deficiency are rare. Pubertal development appeared to be perfectly normal and gynaecomastia was not a significant problem.