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Assessment of ACTH-Adrenal Activity and Diagnostic Value of Plasma ACTH.

In primary adrenal insufficiency plasma ACTH values are 5-10 times above the upper normal limit (80-100 pg/ml) and allow a confirmation of the diagnosis even during substitution therapy. Clearly elevated ACTH levels (mean 720 pg/ml) are found in 50% of treated CAH patients. In cushing's disease ACTH concentrations at or above 500 pg/ml of plasma are found. The ACTH-response to a 3 hour metyrapone test was compared between 18 steroid treated patients (29 tests) and 21 tests performed for growth retardation. The tests were analysed based on the following criteria: basal ACTH, < 50-100 pg/ml, increase ≥ 50 pg/ml, maximum ≥ 100 pg/ml. Cortisol basal value 6-13 µg%, compound-S increase ≥ 4 µg%. In steroid treated patients a normal function was found in 4 tests and signs of incomplete recovery in 10 tests. In 6 tests a partial insufficiency was diagnosed. A complete suppression was found in 4 tests. ACTH adrenal function during and after steroid treatment appears to be largely unpredictable. The metyrapone test is valuable in assessing ACTH adrenal function in suspected secondary insufficiences. Plasma ACTH concentrations without stimulation are helpful for the diagnosis of primary adrenal insufficiency of cushing's disease and for the biochemical control of congenital adrenal hyperplasia.

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Quantitative and qualitative analysis of LH-RH test in normal and endocrinologically sick pre-adult subjects.

The pattern of LH-RH evoked (50 µg/M²i.v.) release of LH and FSH was analyzed quantitatively as well as qualitatively in 123 normal and in 286 endocrinologically sick pre-adult subjects to characterize the functional state of their gonadotostat. The common methods applied to assess this functional state are not adequate enough to differentiate the quantitative and qualitative patterns of response, and therefore a comparative examination was carried out for the peak increment, net increment, area under the time-response curve till the peak value and the cumulative response, ie, the total area under the time-response curve in each subject. As almost all the parameters were just-normally or log-normally distributed, statistical assessment was based on non-parametric Mann and Whitney test. The cumulative response and median comparison gave more meaningful data, based on the magnitude and shape of the release pattern, for an accurate differential diagnosis.

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Treatment of precocious puberty (PP) with DANAZOL.

1. DANAZOL (D), a weak androgenic agent, provokes changes in endometrium. In presence of D, organotypic cultures of endometrial biopsies obtained on day 12 of menstrual cycle in 10 adult females showed epithelial involution with persistance of mitochondrial activity suggesting a direct effect of D on endometrial tissue.

2. The effects of D have been studied in 5 girls with idiopathic (3 cases) or tumoral (2 cases) PP treated for 3, 6, 6, 19 and 40 months. At start of therapy, average chronological age was 6.8 years and average height age (HA) was 8.6 years. Average advance in bone age (BA) was 2.8 years. One patient (aged 5) had already experienced menarche. When on D, menstruation never occured, breast development ceased (3 cases) or regressed (2 cases) but pubarche slightly increased in all cases. In 4 patients treated for 6 months or more mean ΔHA/ ΔBA was 1.1., suggesting that B.A. increament was slowed. FSH, LH and E_2 levels were not consistently modified.

Tolerance of D was good except for transient androgenic manifestations when on high doses (≥400 mg/day). Adrenal function was not depressed when evaluated with ACTH or lysine vasopressine tests. Prolactin levels remained in normal range. These results show that : 1. besides its antigonadotrophic activity, D, a weak androgenic agent, presents direct effects on endometrial tissue. 2. D may be useful in the management of PP in girls with minimal side effects at the daily dose of 200 mg.

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Circadian variations of immunoreactive gonadotropins and gonadotropin-releasing hormone (Gn RH) excretion in timed urinary samples.

Timed urinary collections were obtained in normal and diabetic children. Urinary hormones excretion was measured in samples collected from 8 to 12 a.m., 12 to 4 p.m., 4 to 8 p.m. and 8 to 8 a.m. The results were corrected for each period using urine volume and were given in mIU or ng per 1 hour. In prepubertal and pubertal children, the values of gonadotropins and GnRH were found to be significantly higher (mean 2-3 fold increase) in urinary samples collected during the morning than in those obtained during the night. As plasma gonadotropins were previously shown to be increased during the night, the increase of these hormones excretion in urine might be delayed according to the half life and renal metabolism of these hormones.

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Diurnal variations of LH, FSH and PRL in normal children and in 3 girls with premature thelarche before and after cyproteroneacetate therapy (CA).

In prepubertal boys and girls, a sleep-related increase of FSH occurred, followed by a sleep-related increase of LH at puberty. These rhythms developed later in boys than in girls. Concomitantly to the occurrence of sleep-related gonadotropin rhythms, an increased PRL-release was always present in all children. The hormonal variations of 3 girls with premature thelarche are compared to those of normal developed children. All of them demonstrated advanced bone-age of more than 2 years. In comparison, increased basal FSH and normal basal LH levels were found together with a sleep-related increase of both hormones. After LRH a more pronounced response occurred. After a 4 month period receiving daily 150 mg/m² body surface CA orally, LH was depressed without increasing levels at sleep, whereas FSH still increased during sleep. Basal PRL levels increased from 5-7ng/ml to 20-25ng/ml. An interfering action of CA at hypothalamic and/or pituitary levels has to be discussed as well as the observations that high PRL levels demonstrate an antigonadotropic effect too.

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Investigations on "EARLY NORMAL PUBERTY"

"Early normal puberty" (H. Seckel, 1951) is no pathological form of sexual development but an extreme variant of the norm. This is a report on 11 girls and 2 boys. First pubertal signs, inaccurately remembered in most cases, varied from age 6.25 to 9.0 Menarche occurred with 10.45 ± 0.95 ys. Statural growth, skeletal and sexual maturation were equally accelerated. Mean predicted adult height (acc. to Tanner) was 176.0 cm for the girls, 175.9 cm for the boys. 3 patients meanwhile ceased to grow; their predicted and definite height was 168.8/168 cm; 175.4/174 cm; 172/171 cm, resp.. Thus, adult height is normal and may be slightly supranormal in early normal puberty, - in contrast to children with precocious puberty. The early sexual maturation appears to be triggered by the forced physical development on the whole, manifested by the advanced bone age. Mean difference between chronological and skeletal age was 2.32 ± 0.7 ys. Acceleration of growth and skeletal maturation seems to be caused by increased secretion of hGH. In 3 girls aged 7.9; 9.75 and 12.3 ys we have determined the nocturnal hGH-secretion. Total secretion was significantly enhanced. The highest peaks measured were 157;70;63 ng/ml. Thus, "early normal puberty" appears to be the exact counterpart to "constit. delay of growth and adolescence" where we have stated a relative lack of total hGH-secretion.