41 MAINTAINED CIRCADIAN RHYTHM OF PLASMA-ACTH IN A GIRL WITH NELSON SYNDROME.

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As postulated by Nelson and Sprunt and confirmed by Besser and Landon, Cushing's disease can be subdivided into stages based on plasma-ACTH. All patients supposedly fail to show a normal circadian ACTH-rhythm. Hypothalamo-pituitary function was studied in a girl adrenalectomized at age 12 for Cushing's syndrome with bil. adrenal hyperplasia, in whom Nelson's syndrome developed 2 years later. There was marked sellar enlargement and moderate hyperpigmentation. Plasma-ACTH values at 9:3o, 12:3o, 15:3o, 18:3o, 21:3o, 0:3o, 3:3o and 6:3o were: 3575, 725, 256o, 275o, 288o, 37oo, 59oo and 631o pg/ml (Amersham-Kit). There was subnormal response to consecutive arginine/insulin stimulation for HGH with a peak of 3.6 ng/ml. TSH-values during a TRF-test at o,1o,15, 2o,3o,45,6o and 9o minutes were: 9.3, 11.5, 1o.4, 14.2, 14.5, 11.9, 14.6 and 12.3 uU/ml.
Menstrual periods were normal as were LH- and FSH-responses during LHRF-test. Without aggressive therapy the course was benign so far. It is concluded that ACTH circadian rhythm may be preserved even at an extreme level in children with the Nelson syndrome.

42 PLASMA SOMATOMEDIN ACTIVITY IN FAMILIAL LARON'S DWARFISM.

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Two families are concerned, in both 2 children were affected of severe dwarfism with clinical and biological features usually noted in Laron's cases.
Family 1: Girl 19 year old. Height 125 cm, typical morphology and facies, mild mental retardation.
Boy 6 year old, height o,82. Typical aspect of Laron's dwarf but also retarded and epileptic. Plasma HGH determinations gave high values at several times (3o-4o-6o ng/ml).
Family 2: Girl 18 year of age; height 123. Typical Laron's dwarf morphology and normal mental development.
The boy, aged 16 years, height 12o, showed the same features: Both had high plasma HGH levels (4o-1oo ng/ml). The two boys were treated by HGH therapy for several months without any effect. Before therapy plasma somatomedin ranged 4o-6o and did not improve after HGH. Immunological, electrophoretical studies on plasma GH did not show any abnormality, compared with HGH standard. It is concluded that the 2 families were affected of a primary somatomedin generation deficiency.

43 IN VITRO-MICRO-BIOTRANSFORMATION OF PREGNENOLONE AND PROGESTERONE IN TESTIS BIOPSY MATERIAL OF CRYPTORCHID BOYS.

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Testis biopsy materialswere taken from 1o cryptorchid boys during maldescensus operation, whereas normal materials were obtained from deceased patients. ^{3}H-Pregnenolone and ^{14}C-progesterone were used as substrates. Biotransformation of both substrates to testosterone was found to be diminished markedly in the cryptorchid materials when related to the normals. The normal testis biotransformed pregnenolone in a more pronounced way to the 5α-reduced substances, such as dihydrotestosterone and androstanediol, than did the cryptorchid materials. These differences were less evident using labelled progesterone as a substrate. Here, androsterone was a major metabolite and the yield for the cryptorchid tissues was significantly greater than that for the normals.
In conclusion the cryptorchid testis showed marked differences in the pattern of biotransformation of the labelled steroid precursors.

44 CRITICAL EVALUATION OF ACTH RADIOIMMUNOASSAY FOR CLINICAL INVESTIGATION.

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ACTH radioimmunoassays and steroid assays were carried out on 31 controls and on 85 patients with suspected endocrine disease. In all the patients with suspected Addison's disease and in most cases of suspected congenital adrenal hyperplasia (CAH) or ACTH deficiency, basal or stimulated ACTH levels permitted either confirmation or rejection of the diagnosis. Normal ACTH levels were observed in the 6 patients with untreated Cushing's diseases. After treatment the development of basal ACTH levels and of ACTH response to sequential lysine vasopressine (LVP) tests appeared to be very useful for the detection of pituitary tumors. Simultaneous determinations of 18o pairs of ACTH and cortisol in patients free of hypothalamo-pituitary trouble, of 38 pairs of ACTH and 17 OH progesterone in patients with CAH, of 38 pairs of ACTH and 11 deoxycortisol after metyrapone indicated frequent dissociations between ACTH and steroid levels. This could be related to the differing fluctuation periods as well as the different half lifes of ACTH and steroids. In most cases these results agreed with our previous results using the bioassay but some discordances were observed especially in the course of dynamic tests (LVP, metyrapone, and dexamethasone tests).

Read by Title

45 PROLACTIN RESPONSE TO TRH IN PREPUBERTAL CHILDREN.

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In view of the structural or functional relationships of prolactin (hPR) with other pituitary hormones, its secretory response to TRH was investigated in normal prepubertal children and in children suffering from hypothalamic or pituitary disturbances. hPR was measured by a double-antibody radioimmunoassay using reagents donated by the NIAMD. In ten normal prepubertal children (5 boys, 5 girls) aged 4 to 11 years, the mean basal level was 29,3 ng/ml (range 12-5o). The maximal response to TRH was observed 1o or 2o mn after the IV injection of 200 $\mu g/m^2$ and the mean increment was 42 ng/ml (range 7-78) or 184% of the basal level (range 16-442). In 4 children with hypersecretion of TSH due to primary hypothyroidism, the hPR response to TRH was not significantly different from normal. In 2 children who had undergone surgery for cerebral tumours and whose hGH secretion was deficient, the basal levels and TRH responses of hPR were within normal limits. In 2 others, the pre- and post-stimulatory levels of hPR were steadily higher than 2oo ng/ml. Thus in GH deficient children, hPR secretion may be normal in spite of their structural relationship. The considerably high hPR levels observed in some prepubertal children after surgery for cerebral tumours may be important with respect to their pubertal development.

46 SERUM ANDROGENS, SEX HORMONE BINDING GLOBULIN AND BONE AGE IN JUVENILE DIABETICS.

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In males with diabetes mellitus presenting in childhood, puberty may be delayed. Serum androgens (SA), chronological age (CA), bone maturation (BA) and sex hormone binding globulin (SHBG) capacity of sera were recorded in 58 male juvenile diabetics aged 5.2/12 - 19.3/12. Tanner pubertal rating and SHBG capacities were assessed in all. SA (predominantly testosterone) were measured in 57 by radioimmunoassay and BA were obtained in 46 patients. Taking all the patients together, statistically significant correlations were demonstrable between the following parameters:- CA:SA r= o.75 $p = <.ool$, BA:SA r= o.72 $p = <.ool$ (exponential regression), SHBG:SA r= (-)o.36 $p = <.ol$. On average, androgens rose progressively with CA and BA. The SHBG capacity fell, coincident with increasing BA and rising SA levels. 9 patients had low SHBG capacities suggesting poor binding or failure of protein synthesis. When the ratio $\frac{BA}{CA}$ was plotted vs. SA, 13 patients (28%) aged 8.6/12 - 15.11/12 showed evidence of retarded BA, which in all but 2 coincided with SHBG capacities in keeping with values for prepubertal children. In the older patients of this group, the SA were significantly lower than levels expected for their CA. This data supports the view that retarded BA in some male diabetics is related to low androgen production and changing SHBG capacities.