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Neonatal screening for congenital-adrenal hyperplasia using a microfilter paper method for 17-α-hydroxyprogesterone radioimmunoassay. Experience gained from 22.233 cases.

We examined 22.233 infants born in Emilia-Romagna (Italy). Capillary blood samples for 17-OH-progesterone assay were collected on the 3rd, 4th, 5th, 6th or 7th day of life on filter paper of the same type used for the screening of aminoacidopathy and hypothyroidism. 17-OH-progesterone values were determined using a micromethod modified from that of Pang et Al. 20 pg/disk was considered as a threshold value and called for a second assay, which was performed in 0.18% of cases. Pathologic values of 17-OH-progesterone were confirmed in the serum of 4 neonates. In our population the incidence of 21-hydroxylase deficiency was found to be 1 out of 5.558 cases.

139 C.DACOU-VOUTETAKIS, M.KANARIOU*, E.ROMA*, A.CONSTANTOPOULOS*, M.MANIATI*, C.VRETTOS*. A' Dept. Ped. Athens University. A hypothalamic syndrome characterized by hypernatremia, adipsia, hyperprolactenemia and high threshhold for vasopressin release.

Adipsia with high threshhold for vasopressin release was diagnosed in a 9-year-old girl with episodes of muscular weakness, hypernatremia (Na 162-175 mEq/L) ↑BUN, ↓Hb and ↓platelets, and urine osmolality 800-1400 mOsm/L. The levels of serum prolactin, FSH, LH, and estrogens (306 pg/ml) were high. She was obese with normal linear growth, and mentality, and Tanner II pubic hair. Thirst was not sensed even with serum osm. of 365 mOsm/L Prolactin decreased after hypertonic saline infusion (1640 to 1200 mIU/ml) and after L-DOPA (1600 to 600). Thyroid, and adrenal function, and muscle enzymes were normal. CT brain scans, the last one two years after initial symptomatology, were normal. The forcing of fluids (1500 ml/day) resulted in clinical improvement, normalization of serum Na, BUN, Hb and platelets and the appearance of regular menses. Prolactin, LH, and FSH did not change. The pathophysiologic implications will be discussed. It is postulated that the biochemical findings might have been caused by hypothalamitis (autoimmune?) with selective dysfunction of the thirst center, osmolar receptor-vasopressin release complex and the centers for LHRH and prolactin regulation.

137 J.B. BAUMANN*, A. HÄUSLER*, U.W. OTTEN* and J. GIRARD Kinderspital, Basel and Biozentrum Basel, Switzerland Hypothalamo-Pituitary-Adrenal (HPA) function during development of genetically programed hypertension.

The possibility of an instability of the HPA axis during development of essential hypertension was examined in spontaneously hypertensive rats (SHR) taken as a model of human essential hypertension. Genetically similar normotensive counter-parts WKY) and normal Wistar-rats served as controls. Investigations were performed at 4, 8, 12 and 16 weeks of age. ACTH and corticosterone (B) were measured by RIA. CRF was assayed by RIA of the ACTH released from dispersed pituitary cells in response to 5 - 6 pooled crude hypothalamic extracts compared to 10 mU of vasopressin. B-response to different doses of ACTH from dispersed adrenal cells was age dependent in all 3 strains. In prehypertensive (4 weeks) SHR-rats the B-response to the lowest ACTH-dose was nearly twice that of the controls. No difference of the in vivo B-response to an ACTH-dose of 0,5 mU/100 g was found in any age-group between the 3 strains. 1 min. exposure to ether resulted in a plasma-ACTH-increase which was significantly higher in SHR-rats at 4 weeks of age. B-increase was only slightly elevated compared to controls. These differences were no more obvious at 12 to 16 weeks of age. CRF-activity in unstressed animals showed no difference neither between age-groups nor between SHR and control animals. A temporary instability of HPA-function is thus supported by these findings and a central dysregulation can be assumed.

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Rise in plasma growth hormone in response to exogenous LRH in Klinefelter's syndrome.

In a group of 16 patients with Klinefelter's syndrome (KS) aged from 2 8/12 to 31 yrs, a study was made of the plasma growth hormone (hGH) response to LRH (50 μg/m² i.v.; n=16), TRH (200 μg i.v. n=14) and insulin induced hypoglycemia (0.1 U R.I./kg i.v.; n=6). There was a rise in hGH following LRH from a level below 5 ng/ml during fasting to a level above 8 ng/ml ($p < 0.001$) in 9 (56.3%) of the 16 patients tested. A similar response was found in only 1 of a control group of 15 boys matched for age. TRH stimulation led to a rise in hGH in 1 of the 14 KS patients tested, with none in the control group. Insulin induced hypoglycemia elicited a normal response of hGH in the 6 KS patients tested, from 1.8±0.7 to 16.5±3.7 ng/ml (m±SD, $p < 0.001$). Basal prolactin (Prl) levels were normal in the KS patients (9.4±4.1 ng/ml, m±SD) but the response to TRH stimulation was significantly higher (63.3±40 ng/ml; $p < 0.01$) than that of the control group (30±15 ng/ml). The abnormal rise of hGH following LRH stimulation and of Prl following TRH stimulation denote a disturbance in the neuroendocrine regulation mechanisms of these hormones in KS.

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Histiocytosis X: Neuroendocrine Testing & Growth Hormone Response

The extent of neuroendocrine impairment in 6 cases of disseminated histiocytosis X (HX) & response to hGH therapy in 3 cases was evaluated. Four males & 2 females with biopsy-proven bone & soft tissue involvement, $\bar{X}$ age at onset was 2.3 yrs. Each required chemotherapy & prednisone, 4 skull irradiation. All exhibited neurogenic diabetes insipidus (DI). LH & FSH levels averaged 2.9 & 3.4 mIU/ml prepuberally & rose at puberty in 1 patient. ACTH & cortisol did not respond in 2 cases. Stature was mildly to severely impaired, averaging 2.33 SD below the $\bar{X}$. Basal $\bar{X}$ GH level was 1.52ng/ml. GH deficiency was established with hypoglycemic & arginine stimulation. These cases were treated with hGH 0.08U/kg 3x weekly. Growth rates averaged 3.77cm/yr prior to hGH therapy & 5.41cm/yr with hGH. Growth rates in the 3 cases without GH deficiency averaged 4.42cm/yr. T_4 levels were normal in all cases ($\bar{X}$ 7.5ug/dl). TSH & PRL secretion were stimulated with 100ug TRH (IV). TSH rose from basal $\bar{X}$ of 4.2 (R3-6)mIU/ml to a peak $\bar{X}$ of 21 (R9-42)mIU/ml at 30 min. PRL rose from a basal $\bar{X}$ of 8.7 (R4-20 ng/ml to a peak $\bar{X}$ of 49 (R28-84)ng/ml at 30 min. This data suggests that HX has a selective effect on hypothalamic-pituitary function. TSH & prolactin responses to TRH were normal in all cases. This does not support the hypothesis that HX extensively infiltrates the hypothalamus. Response to hGH, while modest, exceeded growth rates of HX cases without GH deficiency.

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Studies on the mechanisms of stress-induced inhibition of testicular function.

"Psychological" and "physical" stress may inhibit the hypothalamic-pituitary-gonadal (HPG) axis in animal species and man. In addition, the drastic fall in T levels observed during stress may occur without any concomitant fall in plasma LH. This dissociation between LH and T during stress has been investigated and several "in vivo" and "in vitro" experiments performed in adult Sprague-Dawley rats subjected to chronic immobilization stress. In intact or hypophysectionized rats LH-releasing hormone induced a significantly greater release of LH in stressed animals than in normal controls. The sensitivity of the hypothalamic-pituitary axis to circulating T levels was decreased while the testis was relatively less sensitive to exogenous gonadotropic stimulation. Evidence of a blockade in the biosynthesis of T situated beyond cAMP was obtained together with that of an inhibitory factor of pituitary origin, exclusive of endorphins and of other opiate peptides. The action of the factors involved which are likely multifactorial is both extremely rapid and persistant since the effect of immobilization on T release is already apparent 30 minutes after the initiation of stress and persists at least 24 hours after cessation of the exposure to stress.