

5 ACTH AND PROSTAGLANDINS, RECEPTORS IN HUMAN ADRENOCORTICAL TUMORS. J. M. Saez, A Dazord and L. Audi. INSERM-U.34 - Hôpital Debrousse -69322 LYON CEDEX 1

The binding properties of prostaglandin PGE and ACTH, and their action on adenylate cyclase activity (AC) have studied in 12 hormone producing tumors of the human adrenal cortex and compared with those found in the same type of subcellular preparation (20 000 xg) from normal human adrenal glands.

A specific binding of PGE and a stimulation of AC by this hormone and by NaF was obtained in all cases. A specific binding of 125 I-ACTH was also observed in all cases, but ACTH only stimulated AC in six cases. In the other six cases where AC was insensitive to ACTH, the steroidogenesis was not stimulated "in vivo" by this hormone. However these tumors bound specifically 125 I-ACTH $_{1-24}$ and 125 I-ACTH $_{11-24}$, the K_D being similar for both peptides but 100 times lower than the one found in normal adrenal cortex for 125 I-ACTH $_{1-24}$. This results strongly suggests the possibility of a modification or a loss of the receptor site which binds the N-terminal sequence (1-10) of ACTH known as the biologically active part of the molecule.

6 A TEST FOR HETEROCYGOCITY IN CONGENITAL ADRENAL HYPERPLASIA (CAH)

D. Knorr, F. Bidlingmaier, O. Butenandt, K. v. Schnackenberg and W. Wagner. Universitäts-Kinderklinik München, Germany

Presently, there is no conclusive test to detect heterocycosity in CAH. We investigated the increase of 17-OH-Progesterone (17 OH-P) within one hour after intravenous ACTH stimulation with SYNACTHEN and the quotient increase of 17-OH-Progesterone: Increase of Cortisol in 17 normals, 30 heterocycotes, i.e. parents of CAH children and 34 CAH patients with specific radioimmunoassays.

The mean increase of 17-OH-P is 151 ng/100 ml in normals, 450 ng/100 ml in heterocycotes and 11 100 ng/ml in CAH children. Statistically the three mean values are different on the $P < 0,001$ level. Only 13 out of 30 heterocycotes are higher than the highest normal value.

The mean values of the quotient increase of 17-OH-P: increase of cortisol of normals and heterocycotes are also statistically different on the $P < 0,001$ level. 22 out of 30 values of heterocycotes are higher than the highest value of normals. Thus for the present we are able to distinguish about 74% of heterocycotes from the normals.

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7 PLASMA ALDOSTERONE (PA) IN CHILDREN WITH ADRENAL INSUFFICIENCY. M.C.Raux, M.T.Phan-Huu-Trung, M.C. Baron, A.Pappo, F.Girard. (Hôp. TROUSSEAU - Paris)

PA was estimated by radioimmunoassay. Twenty normal subjects aged 5 to 30 years, placed in the supine position, for 2 hours sampled between 8 and 10 a.m., during a normal sodium intake had a mean PA value of 20.6 ± 2.4 (SEM) pg/ml (basal levels). The increase in PA after IM injection of $\alpha 1-24$ ACTH (250 μ g) was 500 to 2000 % (9 subjects) and after five days of low sodium intake (LSI) it was 457 to 1220 % (5 subjects). In 12 infants aged 1 to 12 months, the mean basal PA was 102 pg/ml (range 19 to 171 pg/ml). Among the 20 children with congenital adrenal hyperplasia, 4 salt losers were studied before any treatment during the first month of life, while they were suffering from an acute salt depletion. Their PA were lower than 50 pg/ml. Sixteen 2 to 9 year old patients never had clinical symptoms of salt depletion. While 8 of these were not under treatment, basal PA were elevated (40 to 320 pg/ml). The LSI and the ACTH injection induced variable but limited increases in PA. Since the biosynthesis of Aldosterone appears to be limited, these patients may be considered potential salt losers. When treated with cortisol, the PA levels decreased and a positive correlation ($p < 0.001$) between PA and 17 Hydroxyprogesterone, levels was observed. In 13 of the 17 children with Addison's Disease, PA was lower than 15 pg/ml. Four other patients exhibited normal basal levels and the increases in PA during LSI were 300 to 1100 %, with normal sodium balances. A deficiency progressively affecting diverse adrenocortical functions is discussed.

8 PLASMA ALDOSTERONE (PA) AND EFFECT OF ACTH IN CONGENITAL ADRENAL HYPERPLASIA, 21-OH DEFICIENCY (CAH). J.M. Limal*, F. Bayard** and R. Rappanort*, Hôpital des Enfants Malades*, PARIS, and Hôpital Purpan**, TOULOUSE.

In order to assess the mineralocorticoid adjustment, plasma renin activity (PRA), PA and 17-OH progesterone (17 OHP) were measured by radioimmunoassay in 15 CAH children aged 5 to 16 years on controlled sodium diet, treated exclusively with oral hydrocortisone (F), 20-25 mg/m²/day. Mean baseline PA was above control values of 13.0 ± 7.8 ng/100 ml in 5 non salt losers, group I, PA = 26.4 ± 6.7 ng/100 ml, $p < 0.01$, while PA = 20.3 ± 6.8 ng/100 ml in 10 salt losers, group II (NS with controls). However, among salt losers, we found 4 high PA basal values ranging from 36 to 66 ng/100 ml. Under ACTH stimulation (synacthen 0.25 mg i.m.), PA increased significantly in Group I 30 min. post ACTH, (PA = 44.0 ± 8.7 , $p < 0.01$) and was unchanged in Group II, PA = 20.9 ± 6.4 ng/100 ml, NS with controls (34.9 ± 7.8 ng/100 ml). Elevated PRA in G.I. (3/5 cases) and in G.II (5/10 cases) was associated with increased basal PA. A positive correlation was found between PA and 17-OHP ($r = 0.72$, $p < 0.01$). However, high PA, PRA and 17 OHP returned to normal levels in 4 salt losers given 9 α fluoro-hydrocortisone. In conclusion, F alone adequate for normal growth, was unable to suppress hyperaldosteronism in patients of both groups.

9 DETERMINATIONS OF PLASMA TESTOSTERONE (T), 17-OH ROGESTERONE (17-OHP), ACTH & RENIN ACTIVITY (R.A) IN THE TREATMENT CONTROL OF CONGENITAL ADRENAL HYPERPLASIA DUE TO C-21 HYDROXYLASE DEFICIENCY (C-21 AH). M. David, P. Gilet, L. David. Hôp. Debrousse, Service Prof. Jeune; Hôp. E. Herriot Service Prof. Francois; INSERM U 34, Prof. J. Bertrand, Lyon (France)

These parameters were determined in 34 children and adolescents with C-21 AH, during 2 years period. Blood samples were obtained between 6 and 9 a.m. on fasting individuals after one night of rest at the hospital. Elevated levels of T were observed before treatment or when the glucocorticoid doses were insufficient. In some cases, starting or raising the mineralocorticoid treatment (9 alpha fluorocortisol) was followed by a decrease in T levels. High levels of R. A. were constantly found before treatment, even in the absence of salt losing syndrome. In some cases treated by glucocorticoid and salt, R.A. levels remained elevated: appropriated doses of 9 alpha fluorocortisol induced a marked decrease in R.A. levels. Elevated 17-OH levels were always present before treatment, but frequently failed to normalize under therapy. Important individual variations were observed from day today and in the same day. As far as ACTH is concerned, our data are too inconsistent to take into account this parameter. Regular determinations of plasma T and R. A. allow us a better control of glucocorticoid therapy (our mean dose being 19 mg hydrocortisone/m²/day which is lower than dosages usually published) and of skeletal maturation (however, none of this infants followed since birth are older than two years).

10 PLASMA DEHYDROEPIANDRONE (DHEA) AND TESTOSTERONE (T) IN NORMAL CHILDREN AND IN PATHOLOGICAL SITUATIONS. Pierre C. Sizonenko, Luc Paunier, Marguerite Wyss, Anne-Marie Doret. Clin. Univ. de Pédiatrie, Geneva, Switzerland.

Plasma DHEA and T were measured after column separation by radioimmunoassay, in 125 normal boys aged 5 to 16 years; bone age (BA) was from 4 to 16 years. DHEA rose from 48.1 ± 1.6 (mean \pm SE) at BA 6 years, to 132 ± 19 ng/100 ml at BA 9 years. A further increase was observed at BA 13 years to 316 ± 13 ng/100 ml, contemporary of increase of T from 13 ± 1.8 to 24.6 ng/100 ml, with a steady rise of T to 520 ± 135 ng/100 ml at BA 15 years. In 96 normal girls aged 6 to 16 years (BA from 4 to 16 years), DHEA rose from 31.9 ± 38 (BA 5 years) to 64 ± 8.6 at BA 6 years, then to 123 ± 47 at BA 10 years. At BA 13 years, mean DHEA was 492 ± 84 ng/100 ml. This last increase was contemporary of T increase from 18 ± 3.3 (BA 10 years) to 33 ± 4 (BA 13 years). In Addison's disease, very low levels of DHEA were found although pubertal development had started. In 6 girls with treated congenital virilizing adrenal hyperplasia, normal to high levels of DHEA and T were observed. In 2 cases with Cushing's syndrome, very high levels of DHEA decreased with therapy to normal or low levels.