49. METYRAPONE-INDUCED DECREASE IN PLASMA CORTISOL, ACTH AND BETA-ENDORPHINE IN THE TREATMENT OF CUSHING'S DISEASE

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In Cushing's disease metyrapone pretreatment facilitates transphenoidal selective microadenomectomy and, additionally, permits referring for neurosurgery cases with severe vascular fragility, psychosis, diabetes and staphylococcical or fungal infections. These complications disappear when metyrapone-induced remission in Cushing's disease is achieved.

Fourteen patients with ACTH-dependent Cushing's disease were investigated. Metyrapone /Ciba-Geigy/ was administered in a dose of 1 to 2 G daily for a period of 6 weeks to 2 years. Plasma cortisol, ACTH and beta-endorphin were measured before and during the metyrapone treatment. Metyrapone caused a dramatic decrease in plasma cortisol in all patients, ACTH in 9 out of 10 and beta-endorphine in 4 out of 5 investigated. Results obtained show that the beneficial effect of metyrapone in Cushing's disease is probably due to its inhibitory action at least in two sites: on the adrenal steroidogenesis and on the overproduction of ACTH and beta-endorphine by the pituitary microadenoma.

50. The changes of human plasma ACTH, immunoreactive(IR)-β-endorphin(end) and cortisol(F) during gestation, labor and delivery

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IR-β-end, ACTH and F from the plasma of 88 pregnant women with spontaneous labor were measuerd. The concentrations of ACTH, IR-β-end and F gradually increased during gestation. There were significant correlations between ACTH and IR-β-end(r=0.79), as well as between ACTH and F(r=0.54) during gestation.Maternal ACTH and IR-β-end concentrations rapidly increased during the course of labor, peaked immediately after delivery at 671±136 and 514±86 pg/ml, respectively, and decreased two hours later. There was a highly significant correlation(r=0.89) between ACTH and IR-β-end during labor.The levels of F were elevated during labor and showed no difference during the course of labor, or two hours later. There was no significant relationship between ACTH and F(r=0.24) during labor. These results suggest that 1) ACTH and IR-β-end are secreted concomitantly, probably by the maternal pituitary gland during gestation as well as in response to the stress of labor. 2) the lack of correlation between ACTH and F is due to the difference in metabolic clearance rate of these hormones during labor.

51. THE SIGNIFICANCE OF THE CONCENTRATIONS OF CORTISOL AND CORTISONE IN SALIVA

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The total concentration of cortisone in plasma is only 10-20% that of cortisol. However the concentration of cortisone in saliva exceeds that of cortisol. The possible causes of this have been examined by rapidly changing the concentration of cortisol in blood (by administration of oral cortisol, synacthen or insulin). Changes in the concentrations of cortisol and cortisone in saliva and in the bound and free fractions in the plasma were studied. Sixty minutes after the injection of synacthen into 4 normal subjects the total concentration of cortisone in the plasma was virtually unchanged but the cortisol had increased by 163% (range 67-256%). Salivary cortisone had increased by 309% (range 170-429%) and salivary cortisol by 600% (range 430-800%). At this time the salivary cortisone was 5-10 x greater than the concentration of free cortisone in the plasma. It is concluded that salivary cortisone is derived largely from plasma free cortisol.