Symposium IV. Metabolism of Steroids

Studies on the Cortisol Metabolism in Children

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Although it has been reported that cortisol metabolism in children was different from one in adults, much unknown is still remained in its details. This time, we mentioned about the characteristics in children through our studies on the cortisol metabolism.

Following intravenous administration of cortisol-4-^{14}C, urinary main cortisol metabolites were fractionated by paper-chromatography into six fractions; THE, Allo-THF, THF, cortolones, cortols and high polar fraction (H.P.) as what we term. The increase of 11-ketonic metabolites was found and "H.P." fractino was of significantly quantitative importance in older children to be compared with adults. In newborns, free high polar metabolites occupied the most principle parts of cortisol metabolites and became the more prominent, the younger and more premature babies were. 3β-hydroxy metabolites were very low in newborns. The ratio of THE among them comparatively rapidly elevated during newborns, corresponding to the decrease of "H.P." fraction, but THF and Allo-THF did not increase until 4 to 5 months of age. Therefore, 11-Keto and THF ATHF attained to maximal valves at one to two months of age. The ratio of 3β, 20 hydroxy metabolites was comparatively constant in all ages.

In thyroid disorders, no definite increase of 11-ketonic metabolites as were found in adults was found in hyperthroidism, but the decrease of Allo-THF and the increase of "H.P." fraction was remarkable in hypothyroidism. The increase of 11-hydroxy metabolites and the decrease of "H.P." fraction were found in simple obesity. No significant alteration was noticed in subjects receiving corticosteroids inspite of the marked decrease of C.P.R. In adrenal disorders, the increase of 11-hydroxy metabolites was remarkable in adrenal cancer but no significant changes were found in Addison's disease and congenital adrenal hyperplasia.

No difference was disclosed in plasma half-life of cortisol between infants and older children. The administration of ACTHZ had no influence on it. Values of plasma free cortisol at 8 hours after the intramuscular injecitons of ACTHZ (10 u. in infants and 80 u. in older children) were significantly higher in infants than in older children. Therefore, it is suspected that the adrenocortical reserve is better in infants than in older children.

The daily production rate of cortisol (C.P.R.) per m^2 of body surface area was somewhat higher in infants than in older children. C.P.R. was extremely low in subjects who had received corticosteroids for long periods. In simple obesity, C.P.R. was not different from one in normal subjects per kg. of body weight but was somewhat higher per m^2 of body surface area. C.P.R. was not different from one in normal subjects in hypothyroidism but was over double compared with normal mean value in hyperthyroidism. In congenital adrenal hyperplasia due to 21-hydroxylase deficiency, C.P.R. was extremely low in salt-losing type, but were moderately reduced in simple type. C.P.R. was within normal range in compensated type of Addison's disease inspite of lack of ACTH response.

We have used about one third of conventional doses in the maintenance therapy in these adrenal disorders on the basis of our measuring cortisol production rate in children. The result is that all patients have been well controlled without stunted growth or complicated infection.