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Increased Plasma 17-ketosteroid Concentration in Congenital Adrenal Hyperplasia. (20322)

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Although there have been numerous studies of urinary 17-ketosteroid excretion in congenital adrenal hyperplasia(1-4), no data appear to be available on plasma concentration of 17-ketosteroids. Previous attempts to measure endogenous 17-ketosteroids in peripheral blood have resulted either in loss of the steroid during fractionation of plasma(5) or in overestimation of the material extracted(6). A method has recently been developed permitting estimation of endogenously produced 17-ketosteroids in peripheral plasma(7). Accordingly the plasma of normal adults and of patients with congenital adrenal hyperplasia has been investigated.

Methods. Oxalated or heparinized venous blood was collected. Ether extracts from acid-hydrolyzed whole plasma (10% HCl) were made and chromatographed on magnesia-silica gel columns, after which the residues were subjected to a micro-Zimmermann reaction(7). Optical density measurements were related to a calibration curve made with dehydroepiandrosterone acetate and the results expressed as μg 17-ketosteroids per 100 ml plasma. The spectrophotometric curves were done on the Zimmermann color of the residues prepared as described above, using a Beckman DU spectrophotometer (light path 1.0 cm, final vol. 0.5 ml). Recoveries of pure androsterone added to plasma samples carried through the extraction procedure varied between 85 and 100%. No 17-ketosteroids could be detected in the plasma of a gonadectomized-adrenalectomized adult. Prepubertal children were found to have plasma values of <3 μg %.

Results. Fig. 1 shows spectrophotometric curves of the Zimmermann reaction done on plasma steroid residues of a normal man age 35 years, and a girl with untreated congenital adrenal hyperplasia age 13 years. The maxima at approximately 520 mμ are noteworthy,

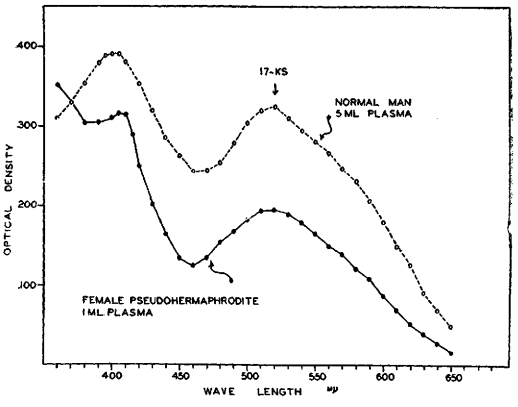

FIG. 1. Spectrophotometric curves of the Zimmermann reaction on plasma residues from a man age 35 years and a girl with congenital adrenal hyperplasia age 13 years (case Gr).

TABLE I. Plasma and Urine 17-Ketosteroid Values.

Patient	Sex	Age, yr	Diagnosis	Neutral 17-ketosteroids Plasma, μg/100 ml	Urine, mg/24 hr
Gr.	♀	13	Congenital adrenal hyperplasia	360	300
Ci.	♂	7	" " "	80	29
An.	♂	8	" " "	80	49
Gu.	♀	6	" " "	88	42
15 adult ♂ controls		19-35	Normal	74 ± 7*	9-17

* Mean ± stand. error of the mean.

since 17-ketosteroids absorb maximally in this spectral range. The significance of the maxima at 405 mμ is not known at present.

Table I presents quantitative data on the concentrations of plasma 17-ketosteroids and urinary 17-ketosteroid excretion in 4 children with untreated congenital adrenal hyperplasia as compared with 15 normal men. It will be noted that patient Gr., a female pseudohermaphrodite, has 17-ketosteroid concentrations in plasma and urine very greatly in excess of the values shown by the younger boys with congenital adrenal hyperplasia. The reason for this difference is not known, although it has previously been observed that the urinary excretion of 17-ketosteroids in this disease may show a marked increase at the time of epiphyseal closure(8). It is apparent that the plasma as well as urine 17-ketosteroid concentrations of these children are considerably in excess of the mean value for normal adult males.

When patient Ci was given 50 mg of cortisone per day by mouth, his plasma 17-ketosteroid concentration fell to values of <16 μg %, and urine values to <8 mg per day.

Discussion. The observation that peripheral plasma 17-ketosteroids are elevated in untreated cases of congenital adrenal hyperplasia and fall with cortisone therapy is of interest in view of what is presently known about plasma 17-hydroxycorticosteroid concentrations. Nelson(9) and Kelley *et al.*(10) have noted that plasma 17-hydroxycorticosteroid concentration is abnormally low in untreated cases of congenital adrenal hyperplasia, and rises to normal values when cortisone therapy is begun. Thus, there appears to be a reciprocal movement of plasma concentrations of 17-ketosteroids vs. 17-hydroxycorticosteroids when patients with this disease are treated with cortisone.

Summary. Measurements of peripheral plasma 17-ketosteroids were made in 15 normal men and in 4 children with untreated congenital adrenal hyperplasia. The 4 children showed plasma values equal to or in excess of the values shown by the men. When one of the children was treated with cortisone, plasma 17-ketosteroid concentration fell to values far below the adult level.

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