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Pituitary-Adrenal Function in Congenital Heart Disease

By

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Pituitary-adrenal function has been studied in children suffering from congenital heart disease. In non-cyanotic patients no alterations were found. In patients with cyanosis, especially after the age of ten, the excretion of ketogenic steroids decreased but following metyrapone administration it rose normally. The plasma cortisol level was normal. In some cases, under the effect of insulin hypoglycaemia, the rise in plasma growth hormone was subnormal. 17-ketosteroid excretion as related to age was low in these patients. The findings suggested a decreased pituitary function in a number of cases of cyanotic heart disease.

In healthy individuals the amount of glucocorticoids secreted by the adrenal gland is proportionate to body size, to weight and body surface. If studied under standardized conditions, the plasma cortisol level is constant throughout childhood with the exception of the first weeks. Excretion of 17-ketosteroids remains unchanged up to the age of 8 to 10 years when it gradually reaches adult values.

In congenital heart diseases, growth and development are mostly retarded and onset of puberty is somewhat delayed. Post mortem findings show that the adrenal glands are often atrophic [1]. Our aim was to study to what extent the changes in adrenal function corresponded to the peculiar growth and developmental pattern of children with congenital heart disease.

MATERIAL and METHODS

The subjects studied were divided in 3 groups.

1. Healthy children 3—14 years of age (n = 48).

2. Cases of congenital heart disease without cyanosis, 3—16 years of age (n = 13).

3. Cases of congenital heart disease with cyanosis, 4—17 years of age (n—20).

None of the patients had congestive heart failure. In each of them the excretion of 17-ketosteroids (17-KS) and ketogenic steroids (KGS) was estimated in the 24-hour urine [2]. In some cases the metyrapone test was also performed, in the following way.

1st day: urine collection

2nd day: 300 mg/sq.m of metyrapone every 4 hours

3rd day: urine collection

In 21 healthy and 19 cyanotic patients the plasma 11-OH steroids were determined by a fluorimetric method [3]. Since the plasma 11-OH-steroid level and KGS-

excretion were mostly estimated at different times and often in different individuals, the results are presented separately.

In some cases the plasma growth hormone level was also estimated in the fasting state and 30 and 60 minutes after intravenous insulin administration (0.1 U/kg). Growth hormone was assayed by the coated charcoal method [4].

Results

In patients suffering from cyanotic congenital heart disease, KGS excretion as related to body surface or weight was less than in normal subjects. This tendency, although appearing earlier, was most marked at the age above 10 years (Fig. 1). In non-cyanotic cases of congenital heart disease KGS excretion was found to be normal.

Following metyrapone administration in healthy individuals KGS excretion increases two to four times. In cyanotic children, even in those exhibiting a very low basal KGS excretion, the response to metyrapone was satisfactory (Fig. 2).

The plasma 11-OH-steroid level in the healthy control group (30.1 $\pm$ 8.3 μg/100 ml) was somewhat higher than the value described in the literature. The difference was due probably to the fact that blood sampling was made after a long, 10—12 hour, period of fasting. The values for the cyanotic group were similar to those found in healthy subjects (27.4 $\pm$ 7.5 ng/100 ml).

17-KS excretion was below 3mg/24 hours up to ten years of age in healthy children; beyond this age the values gradually increased. In patients with cyanotic heart disease this rise occurred in a few cases only, while in the majority the values were still invariably low even at the age of 16 years (Fig. 3). Since there were only a few children above ten years of age in the non-cyanotic group, the question whether an increase of 17-KS excretion occurs normally in these patients had to be left open.

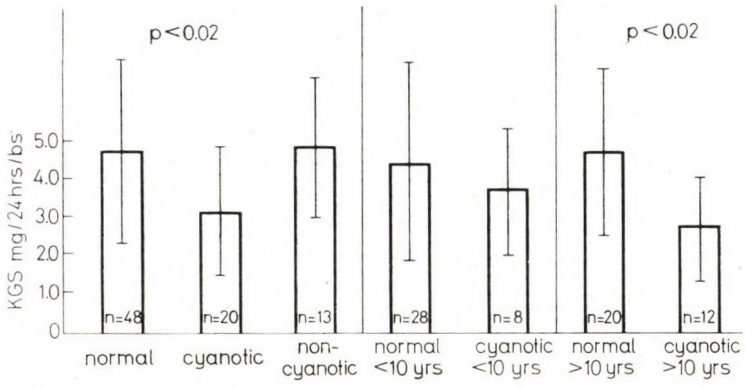

Fig. 1. Daily excretion of ketogenic steroids. mg/sq · m body surface

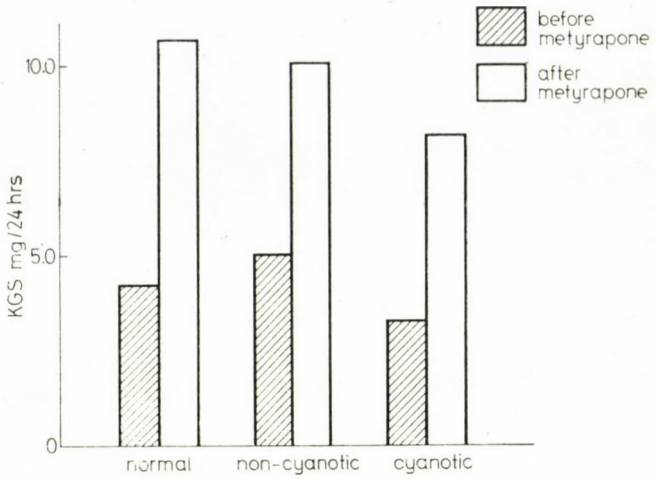

FIG. 2. Change of ketogenic steroid excretion following metyrapone, mg/24 hrs

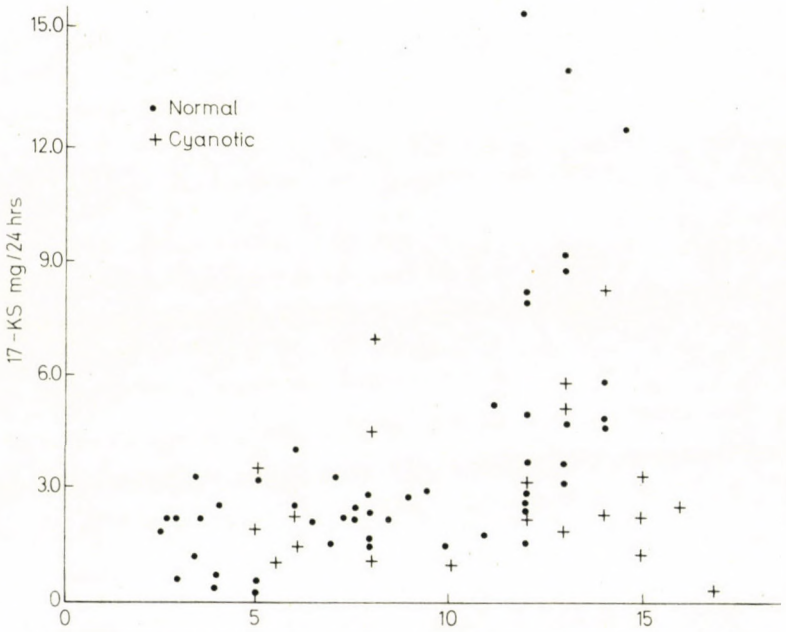

FIG. 3. Daily excretion of 17-ketosteroids as related to age, mg/24 hrs

DISCUSSION

Adrenal function was normal in the non-cyanotic patients.

In children with cyanotic heart disease, KGS excretion as compared to normal controls was lower than would be expected for age, body surface, or body weight. The blood 11-OH-steroid level was, however, normal and glucocorticoid secretion was normally enhanced by metyrapone.

This showed that the pituitary was able to increase corticotropin production and the sensitivity of the adrenal cortex to corticotropin was normal. In some children above ten years of age KGS excretion was extremely low, but here, too, the response to metyrapone was good. There are several possible explanations to account for the decreased glucocorticoid secretion in the presence of a normal plasma cortisol level, such as a diminished conjugation of the glucocorticoids in the liver, or their decreased excretion by the kidneys. Both processes would result in a rise of the blood cortisol level, which in turn tends to lower the hormone production by means of a feed back mechanism. GILROY and MEYER [5] described similar findings in aged patients with cerebrovascular disease and they suggested that the decrease in glucocorticoid secretion was due to a lack of appropriate stimuli from the higher centres to the pituitary. The diminished stimulation of the pituitary may, eventually, have been caused by hypoxia in our cases just as well as in the patients described by GILROY and MEYER [5], resulting in both instances in similar changes.

The growth hormone level in the cyanotic patients also suggested a decrease in pituitary activity after the age of ten. After an insulin load the mean rise of growth hormone in children under 10 years was 36.1 mμg/ml (n = 8), whereas above 10 years of age it was 7.2 mμg/ml (n = 6). In a few cases both the excretion of ketogenic steroids and the growth hormone level were measured. In these instances KGS excretion was lowest in cases where growth hormone secretion was also somewhat low (Table I).

TABLE I

Case	Age years	KGS mg/24 hrs	17-KS mg/24 hrs	Growth hormone mμg/ml*
D. Á.	16	4.6	2.5	17.0
K. J.	14	3.6	2.3	11.0
Sz. L.	13	1.9	1.6	5.5
K. J.	10	0.5	1.0	0
S. M.	15	1.7	2.2	0
G. Zs.	15	2.7	1.3	9.8

* Maximum rise following administration of 0.1 U/kg insulin

The decrease in 17-KS excretion described above agreed well with the findings of LINDE et al. [6] who found that children suffering from cyanotic congenital heart disease reach puberty only after having attained the height of healthy children at the time of puberty. Delayed puberty and decreased 17-KS secretion have been described in subjects living at high altitudes, i.e. under conditions of chronic hypoxia [7].

Since we have examined no cyanotic patient past puberty, it could not be decided whether the described decrease in pituitary function was a transitory or a persistent feature.

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