THE URINARY EXCRETION OF 17-HYDROXYSTEROIDS IN CHILDREN

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The results reported here were obtained as a consequence of routine requests for steroid estimations. Some of the normal figures were obtained privately, but others were obtained from children in hospital, who had no endocrine wasting or similar disorder likely to influence adrenocortical secretion. Most of the requests concerned four types of case: obesity, dwarfism, precocious puberty and adrenal hyperplasia or tumour.

Method

The method of Reddy (1954) was employed. This measures those corticosteroids which have a 17:21-dihydroxy-20-ketone side chain. The two principal glucocorticosteroids which are secreted by the adrenal cortex are hydrocortisone (approximately 85%) and corticosterone (approximately 15%) (Bush, 1953). The principal corticosteroids present in urine are hydrocortisone, cortisone and their metabolites. Both hydrocortisone and cortisone possess the 17:21-dihydroxy-20-ketone side chain, so also do their principal metabolites and therefore these compounds will be measured by the method. Corticosterone lacks the 17-hydroxyl group and it is not measured by this method.

Results

The 17-hydroxysteroids were determined in the 24-hour urines from 94 normal children. The children were divided into two groups, those under 2 years of age, and those over 2. This was done principally because few results were obtained for children at about the age of 2, a most difficult age at which to obtain 24-hour specimens of urine from normal children. The mean excretion of 17-hydroxysteroids in the younger age group was $1 \cdot 2 \pm 1 \cdot 0$ mg./24 hours. In the older group the mean excretion was $3 \cdot 1 \pm 2 \cdot 0$ mg./24 hours (Table 1). The difference between the two groups is highly significant ($P < \cdot 01$). There is no significant difference between the mean figures for excretion for the ages 0-1 year and 1-2 years and the results may be considered as falling into one group. There is probably a rise with age in the older group but the regression is not significant.

Results were obtained from 23 cases of obesity, all of whom were in the older age group. The mean excretion was 3·4 mg./24 hours. In three cases of dwarfism in the younger age group the mean excretion was 0·9 mg./24 hours, and in 15 cases in the older age group it was 2·1 mg./24 hours. In five cases precocious puberty in the earlier age group the mean excretion was 0·7 mg, and in five cases in the older group it was 3·8 mg./24 hours. None of these figures is significantly different from the normal.

TABLE 1
URINARY 17-HYDROXYSTEROID EXCRETION IN NORMAL CHILDREN

Age Last Birthday (years)	Mean 17-hydroxysteroid Excretion (mg./24 hr.)
0– 2	$1 \cdot 2 \pm 1 \cdot 0$
2–17	$3 \cdot 1 \pm 2 \cdot 0$

In the syndrome of congenital adrenal hyperplasia, the excretion of 17-hydroxysteroids is low when determined by paper chromatography (Eberlein and Bongiovanni, 1955). The Reddy method, however, indicates the excretion of normal levels of 17-hydroxysteroids, though in two cases, in brothers, excretion was persistently zero. Furthermore, in three cases to whom ACTH was administered levels rose (Table 2). It must be concluded therefore

TABLE 2
17-HYDROXYSTEROID EXCRETION IN 15 CASES BEFORE AND AFTER ACTH 40 mg./24 HOURS FOR THREE DAYS

Case No.	Diagnosis	Age (years)	17-hydroxysteroids Before ACTH (mg./24 hr.)	17-hydroxysteroids After ACTH (mg./24 hr.)
1	Normal	9	4·3	18·1
2	,,	6	8·8	56·5
3	Dwarfism	1	1·3	11·2
4	,,	5	0·0	8·2
5	,,	6	2·1	17·4
6	,,	6	4·8	41·9
7	,,	6	1·6	26·8
8	,,	8	3·5	26·1
9	,,	8	2·9	20·9
10	,,	10	4·1	24·2
11	,,	11	2·7	31·6
12	,,	13½	1·3	9·6
13*	Congenital adrenal hyperplasia	4 *weeks*	2·6	4·7
14	,, ,,	2	2·3	9·6
15	,, ,,	6½	2·7	12·7

* In Case 13, ACTH 10 mg./24 hours was administered. The highest figures before and after ACTH are given.

that the compounds measured in this condition are not the same as the compounds excreted by normal subjects.

In six children with dwarfism an ACTH test was carried out. A base line figure was obtained for one or two days prior to the test, and ACTH, 20 mg. b.d. was then administered for three days. Table 2 shows the base line figures and the highest figure obtained after ACTH. Excretion usually declined to the control level on the second day after the last dose of ACTH.

The administration of cortisone will cause a rise in 17-hydroxysteroid excretion. In four adults, 50 mg. of cortisone acetate was administered at 8 a.m. and again at 6 p.m., and the 24-hour urine collection commenced at 8 a.m. on the same day. The excretion of 17-hydroxysteroids by the four individuals was 28·8 mg., 28·2 mg., 26·4 mg. and 24·2 mg. The mean base line figure was 2·4 mg./24 hours.

The 17-hydroxysteroids were determined for the first 19 days after menstruation in a girl aged 11 years. The figures in mg./24 hours were 3·3, 4·3, 14·4, 5·6, 4·3, —, 7·4, 7·7, 7·1, 7·8, —, 7·3, 7·6, 9·5, 9·0, 7·0, 6·0, 7·2, 6·7. It will be observed that, except for the high figure obtained on the third day for which there was no obvious explanation, the level of excretion rises to a peak of 9·5 mg./24 hours, and then declines. This peak of excretion occurred on the day following the peak of oestrogen excretion which was determined concurrently.

In a case of Cushing's syndrome in a boy aged 3½ years, the 17-hydroxysteroids were 3·1 mg./24 hours. In a second case due to bilateral adrenal multiple adenomata, the 17-hydroxysteroids were 9·8 mg./24 hours.

Discussion

The method of Reddy is simpler to perform than the 17-ketogenic method of Norymberski, Stubbs and West (1953). The latter method involves the simultaneous determination of the 17-ketosteroids, but since this result is usually required this is a gain rather than otherwise. In this hospital, however, a method similar to the method of Holtorff and Koch (1940) but different from that employed in the determination of 17-ketogenic steroids has been in use since 1940. An independent method of 17-hydroxysteroid determination was therefore of value. Reddy (1954) gives the normal adult range of 17-hydroxycorticosteroids as 1·1-10·7 mg./24 hours with a mean of 4·7. The smaller excretion in children must be due to size, since blood levels are similar (Ely, Raile, Bray and Kelley, 1954). It is of some importance that the upper limit of normal is lower in children since in Cushing's syndrome the figures may be only moderately raised, or, as in one of the cases referred to here, within the normal range. The difficulties of interpretation of ACTH tests have been discussed by Prunty (1956). Since it is not permissible to experiment with normal children by administering ACTH it is hardly possible to obtain genuine controls, and only two cases to whom ACTH had been given therapeutically were considered to be normal controls (Table 2). The response in Case 2 is striking, and it is of interest that the base line figure here is high. The 17-ketogenic steroids after ACTH in this normal child reached 70 mg./24 hours, a figure which matches the response to ACTH in the cases of Cushing's syndrome due to adrenal hyperplasia described by Prunty.

In the cases of dwarfism (who were given ACTH from the same batch) it is clear that the response is variable, though it is possible that the response varies directly with the base line figures.

The normal excretion of 17-hydroxysteroids in one of the cases of Cushing's syndrome (the 17-ketosteroids were moderately raised) reveals the limitations of laboratory methods in this condition. Since in children tumours of the adrenal cortex and not hyperplasia are usually the cause of the syndrome, it is probably true that laboratory investigations can confirm the clinical diagnosis but cannot exclude it.

The 17-hydroxysteroids may also be of value in the diagnosis of Addison's disease and an ACTH test is of importance here. Otherwise it may be concluded that apart from Cushing's syndrome and Addison's disease, both rare disorders in childhood, the clinical value of 17-hydroxycorticosteroid determinations is limited.

Summary

The urinary excretion of 17-hydroxysteroids by normal children and by children attending hospital for obesity, dwarfism, precocious puberty and adrenal hyperplasia has been determined. The clinical value of this determination is discussed.

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References

Bush, I. E. (1953). *J. Endocr.*, **9**, 95.
Eberlein, W. R. and Bongiovanni, A. M. (1955). *J. clin. Invest.*, **34**, 1337.
Ely, R. S., Raile, R. B., Bray, P. F. and Kelley, V. C. (1954). *Pediatrics*, **13**, 403.
Norymberski, J. K., Stubbs, R. D. and West, H. F. (1953). *Lancet*, **1**, 1276.
Prunty, F. T. G. (1956). *Brit. med. J.*, **2**, 615, 673.
Reddy, W. J. (1954). *Metabolism*, **3**, 489.
Holtorff, A. F. and Koch, F. C. (1940). *J. biol. Chem.*, **135**, 377.