

Adrenaline and Noradrenaline Output in Urine After Unilateral and Bilateral Adrenalectomy in Man

By

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The catechol amine output in urine in man is normally about 1/5 adrenaline and 4/5 noradrenaline. This proportion is in good agreement with the relative concentrations recently found in peripheral blood by WEIL-MALHERBE and BONE (1953). The adrenergic nerves in the vessels and in the visceral organs probably represent the most important source of noradrenaline in the urine. Assuming the same concentrations of noradrenaline in human organs and tissues as in the cow or the sheep the total store in the body can be estimated at about 2 mg. Since human suprarenals contain a total amount of about 1 mg noradrenaline (EULER, FRANKSSON and HELLSTRÖM 1954) some of the urinary noradrenaline might be expected to come from this source. Adrenaline, on the other hand, is chiefly derived from the suprarenals (about 6 mg), for the tissues and organs contain only relatively small amounts of adrenaline (0.1—0.2 mg).

In the present report the urinary output of adrenaline and noradrenaline before and after adrenalectomy has been measured in an effort to evaluate the contribution made by the suprarenal glands in the urinary excretion of both catechol amines.

Material and Methods.

Urine was collected for periods of 24 hours from patients in the surgical ward of the Karolinska Hospital before and various times after adrenalectomy. Part of the urine was also used for 17-ketosteroid analysis (HELLSTRÖM et al., 1952.)

The catechol amines were prepared by adsorption on aluminum hydroxide according to EULER and HELLNER (1951) and the amines assayed biologically on the cat's blood pressure and the fowl's rectal caecum (EULER 1949).

The error of any single figure can be estimated at about $\pm 10\%$ for noradrenaline and about $\pm 25\%$ for adrenaline. No corrections have been made for the loss during the preparation of the extract, which amounts to about 25% .

Patients selected had cancer of the prostate or breast or malignant hypertension.

Adrenalectomy was performed unilaterally in 2 patients, bilaterally in 2 stages in 4 and bilaterally in 1 stage in 9 patients. Postoperatively the patients were maintained on 25 (—50) mg cortisone per day.

Results.

The urinary excretion of adrenaline was not altered by unilateral adrenalectomy (table I). However, after total adrenalectomy the adrenaline output is markedly reduced. The excretion figures are so low that the exact excretion rate is difficult to estimate. If, however, the actual excretion rate had fallen to zero a certain number of negative figures should have appeared due to the error in the estimation method. Since this was not the case it is reasonably certain that a small amount of adrenaline is still excreted after total adrenalectomy.

The urinary output of noradrenaline did not change after unilateral adrenalectomy. Although the noradrenaline figures varied a great deal after bilateral adrenalectomy, the highest figures were greater than those before in 10 of 14 cases suggesting an alteration of the noradrenaline output. When the means are compared the significance of the difference is low ($P = > 0.1$). Although high figures of noradrenaline were frequently observed after bilateral adrenalectomy, a lowering of the noradrenaline excretion after adrenalectomy was seldom seen.

Comment.

Although the disease and post-operative treatment of the patients may have influenced the results in various ways there seems to be little doubt that the adrenaline excretion rate was significantly reduced after complete adrenalectomy. The most plausible explanation for this finding is that the pre-operative

Table I.

Catechol amine output in urine before and after unilateral or bilateral adrenalectomy.

Average excretion figures in *italics*. Figures within brackets denote number of estimations over time period in days.

Subject	Age, sex	Adrenaline excretion μg per 24 hours			Noradrenaline excretion μg per 24 hours			Diagnosis
		Before	After adr.ect.		Before	After adr.ect.		
			unilat.	bilat.		unilat.	bilat.	
A. L. A. . .	50 F	8.8 (1/2)	9.6; 11 10.3 (2/5)	—	26	27; 29 28	—	Ca. mam.
S. S.	38 M	3.6; 4.8 4.2 (2/9)	3.7 (1/3)	—	44; 64 54	40	—	Hypertens.
B. G. A. . .	20 M	3.0—9.8 5.2 (6/8)	3.3—9.3 6.1 (6/16)	0.78 (1/9)	9.4—51 27	11—68 36	25	Hypertens.
D. A. E. H.	37 F	2.4 (1/1)	2.1 (1/3)	0.55 (1/1)	7.2	11	22	Ca. mam.
C. M.	46 F	5.0—10 6.9 (3/10)	2.1 (1/6)	0.68 (1/8)	25—26 26	8.9	20	Ca. mam.
N. R. N. . .	45 M	0—12 6.4 (6/7)	1.0—9.9 6.5 (5/21)	0—4.0 1.6 (14/220)	29—70 46	15—82 37	6—91 46	Hypertens.
J. E. W. . .	68 M	—	—	0—3.6 1.9 (6/23)	—	—	25—116 78	Ca. prost.
N. I. H. . .	66 M	2.6—5.1 3.7 (4/8)	—	0—1.9 0.59 (11/190)	18—35 28	—	1.7—109 36	Ca. prost.
J. H.	66 M	1.6; 3.5 2.6 (2/14)	—	0.49—2.3 1.8 (4/24)	60; 79 70	—	46—197 107	Ca. prost.
E. O. K. . .	63 F	5.2; 6.0 5.6 (2/13)	—	0.67 (1/3)	22; 43 33	—	100	Ca. mam.
N. K. N. . .	53 M	0—12 5.2 (3/5)	—	0.65—7.7 4.1 (13/34) 0.2—3.4 0.7 (5/288)	30—38 34	—	29—104 62 33—77 60	Hypertens.
K. S.	60 M	5.5 (1/5)	—	0—2.8 0.80 (12/95)	26	—	7—114 43	Ca. prost.
K. E.	64 M	2.4; 5.0 2.7 (2/10)	—	0—4.3 1.3 (15/44)	32; 69 51	—	8—135 64	Ca. prost.
T. O.	67 M	3.3—7.8 5.6 (4/9)	—	0—3.6 1.1 (7/95)	56—113 72	—	25—100 51	Ca. prost.
E. A. S. . .	55 M	8.2; 9.7 9.0 (2/5)	—	0—2.1 0.51 (9/95)	64; 79 72	—	17—132 52	Ca. prost.
m (average) =		5.4 ± 0.52	5.1	1.0 ± 0.13	41 ± 5.2	27	54 ± 7.4	

adrenaline secretion is predominantly derived from the suprarenal medulla. On the other hand there is good evidence for a small persistent secretion of adrenaline even after adrenalectomy. This is most likely due to the production of adrenaline in chromaffin cells outside the suprarenal gland. It should be recalled that most organs contain in addition to noradrenaline small quantities of adrenaline (EULER 1951) and certain amounts may also be present in chromaffin cell groups along the large abdominal vessels.

It is somewhat surprising that the adrenaline secretion is not altered by unilateral adrenalectomy. The number of cases is small, however, and some hypersecretion from the remaining gland during the post-operative period cannot be excluded, especially since post-operative stress often raises the adrenaline output (FRANKSSON, GEMZELL and EULER 1953).

Three of four patients with hypertension were subjected to bilateral adrenalectomy. No particular features as regards the adrenaline or noradrenaline excretion before or after the operation were noted as compared with the other cases. Clinical improvement was noted in two of these patients after a period of several months (EJRUP 1953). In one patient with hypertension (not included in the table) the pattern of catechol excretion before operation differed from the others. On four occasions pre-operative urinary extracts caused only a marked fall of blood pressure in the test cat. This patient died in shock two days after operation. The nature of the depressor agent or the cause of the shock was not established.

In two patients it was observed that the noradrenaline excretion figures gradually diminished shortly before death (7–13 μg per 24 hours).

An interesting shift in the adrenaline excretion after bilateral adrenalectomy was observed in one patient with hypertension. During the first 5 post-operative weeks the average adrenaline excretion figure was 4.1 μg per 24 hours which is within the normal range. After this time a rather striking fall in the adrenaline secretion to an average of 0.7 μg per 24 hours was noted which persisted over a 10-month-period of observation. No definite alteration in the noradrenaline secretion occurred.

It is of some interest to compare the pre-operative catechol excretion figures with those of a group of hospitalized patients with minor ailments. In 21 estimations on seven such patients

the adrenaline output was $4.1 \mu\text{g}$ per 24 hours (S. D. = 1.43) and noradrenaline $42 \mu\text{g}$ (S. D. = 20), the figures thus showing a good agreement with the pre-operative values reported here.

Summary.

1. Unilateral adrenalectomy in two patients did not significantly alter the output of adrenaline or nor-adrenaline in the urine.

2. After bilateral adrenalectomy the adrenaline output fell from $5.4 \pm 0.52 \mu\text{g}$ per 24 hours to $1.0 \pm 0.13 \mu\text{g}$ per 24 hours (mean of averages in 14 patients).

3. The output of noradrenaline was frequently increased after bilateral adrenalectomy.

4. The results indicate that most of the adrenaline excreted in the urine is derived from the suprarenals, while noradrenaline comes from other sources, presumably the adrenergic nerves.

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