Table II. Kidney and body weights of the same animals of which enzyme activities are presented in the Figure

Treatment	Sham-operated	Cortisone acetate 0 mg	0.1 mg	0.5 mg	2.5 mg
No of mice	13	11	12	12	10
Kidney weight (mg ± SEM)	247 ± 11.8	222 ± 13.0	235 ± 8.2	259 ± 8.6	292 ± 13.2
Body weight (g ± SEM)	25.8 ± 1.00	24.9 ± 1.55	25.8 ± 0.97	25.0 ± 0.91	26.5 ± 1.48

The kidney weight of animals given 0.5 mg and 2.5 mg cortisone acetate was significantly increased.

conversely, administration of hydrocortisone resulted in a sustained decrease in incorporation rate[8].

In our experiments, removal of the adrenals, i.e. depriving the mouse of the normal level of circulating steroids, increased the activity of kidney histidine decarboxylase, suggesting that this hormone level exerts a restraining influence on this particular enzyme activity. This view is born out by the effects of cortisone administration, whereby histamine formation is reduced in a dose-related manner. Indeed, with the largest dose used, histidine decarboxylase activity was lowered to about 5% of the control value, a degree of inhibition that has previously been reported only by the injection of testosterone, under the influence of which the kidney enzyme activity nearly disappeared[9].

The alterations seen in ornithine decarboxylase activity were biphasic; a small dose elevated the activity, whereas on increasing the dose of cortisone the activity decreased. In cases in which the activities of decarboxylases of histidine and ornithine are altered, the levels have been reported to change in an inverse relationship, or merely either of the enzyme activities is involved[3,5].

The kidney weight deserves comment. Cortisone injections in adrenalectomized mice increased the weight of the kidney in a dose-dependent manner, whereas the body weight was not increased. The cortisone stimulated kidney became even larger than that of the sham-operated animals. We did not examine the kidney histologically or for specific indications of tissues growth. Nevertheless, it is noteworthy that the considerable increase in kidney weight was not accompanied by induction of any measurable rise in ornithine decarboxylase activity which otherwise is often seen in tissue hyperplasia.

Summary. In adrenalectomized mice, cortisone inhibited histidine decarboxylase of the kidney in a dose-related manner. The effect of cortisone on ornithine decarboxylase was diphasic: small doses elevated, high doses inhibited.

ANNE CHARLOTTE ANDERSSON,
S. HENNINGSSON and
ELSA ROSENGREN[10]

Institute of Physiology, University of Lund, S-223 62 Lund (Sweden), 4 March 1975.

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Effects of Oophorectomy and Sexual Hormones on Norepinephrine and Epinephrine Urinary Excretion

In previous papers[1,2] the existence of cyclic variations in the norepinephrine (NE) and epinephrine (E) urinary excretion during the sexual cycle of the female Wistar rat was proved. We attribute these variations to the changes in the secretion of the sexual hormones.

In order to verify this hypothesis, we will now proceed to the study of the effects of oophorectomy and the administration of sexual steroids: estradiol benzoate (EB), progesterone (P) and testosterone dipropionate (TD) on the catecholamines urinary excretion.

Material and methods. Female Wistar rats weighing 170–220 g were divided into the following groups: a) control rats in diestrus; b) oophorectomized; c) oophorectomized rats injected with EB, 4 µg daily; d) oophorectomized rats injected with P, 500 µg daily and e) oophorectomized animals injected with TD, 500 µg daily. After the surgical operations, steroid hormones were injected s.c. for 7 days and then, the experiments were performed. The animals were placed in metabolic cages and fed with a mixture of bread, milk and water ad libitum, for 12 h of light-darkness cycle. Samples of 24 h urine were collected on HCl 6 *N*. Urinary catecholamines were extracted by the chromatographic method of VON EULER and LISHAJKO[3] and evaluated by the fluorometric technique of COHEN and GOLDENBERG[4]. The results are given in µg/kg/24 h ± SEM and were analyzed statistically using Student's *t*-test. The urinary NE/E relationship was also studied in the different groups.

Results. Table I shows that the oophorectomy did not change the NE elimination as compared with the control animals, but it did increase E excretion ($p < 0.001$), with the consequent fall of the NE/E relationship. The

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Table I. Effects of oophorectomy and the administration of sexual hormones on urinary excretion of norepinephrine, epinephrine and the NE/E relationship.

	Norepinephrine (μg/kg/24 h $\pm$ SEM)	Variation (%)	Epinephrine (μg/kg/24 h $\pm$ SEM)	Variation (%)	NE/E relationship
Control	3.93 ± 0.15 (15)		0.98 ± 0.11 (17)		4.01
Oophorectomized	4.43 ± 0.16 (15)	$+12.7$ [d]	1.45 ± 0.07 (17) [a]	$+47.9$ [d]	3.05
Oophorectomized + estradiol benzoate	3.69 ± 0.16 (16) [b]	-16.7 [e]	1.77 ± 0.07 (17) [b]	$+12.2$ [e]	2.08
Oophorectomized + progesterone	5.08 ± 0.15 (16) [c]	$+14.6$ [e]	1.46 ± 0.05 (14)	$+ 0.3$ [e]	3.48
Oophorectomized + testosterone dipropionate	4.41 ± 0.26 (15)	$- 0.5$ [e]	1.46 ± 0.08 (14)	$+ 0.3$ [e]	3.02

SEM, standard error of the mean; ( ), number of cases. [a] $p < 0.001$ as compared to control. [b] $p < 0.005$ as compared to oophorectomized. [c] $p < 0.01$ as compared to oophorectomized. [d] % of variation as compared to control. [e] % of variation as compared to oophorectomized.

Table II. Urinary excretion of norepinephrine, epinephrine and the NE/E relationship and its variations during the sexual cycle of the rat.

	Norepinephrine (μg/kg/24 h $\pm$ SEM)	Variation (%)	Epinephrine (μg/kg/24 h $\pm$ SEM)	Variation (%)	NE/E relationship
Proestrus	2.51 ± 0.72 (8)	-26.0 [c]	1.17 ± 0.19 (8)	$+25.8$ [c]	2.14
Estrus	3.05 ± 0.30 (12) [a]	-10.1 [c]	0.95 ± 0.19 (12)	$+ 2.1$ [c]	3.21
Metaestrus	3.41 ± 0.56 (8) [b]	$+ 0.6$ [c]	0.82 ± 0.22 (11)	$+11.8$ [c]	3.64
Diestrus	3.39 ± 0.53 (7) [b]		0.93 ± 0.16 (9)		3.92

SEM, standard error of the mean. ( ), number of cases. [a] $p < 0.05$ as compared to proestrus. [b] $p < 0.01$ as compared to proestrus. [c] % of variation as compared to diestrus.

administration of EB in oophorectomized animals caused a decrease in the NE excretion ($p < 0.005$) and the NE/E relationship and an increase in the E elimination ($p < 0.005$). P injection increased NE excretion ($p < 0.01$) and the NE/E relationship, without changing the E excretion. On the other hand, TD did not alter the urinary catecholamines as compared to group b. Table I also shows the percent of the variations of the results.

Discussion. Variations of the catecholamines content in the hypothalamus[5] in other organs[6–8], and in the urinary excretion[1,2] and Table II), take place during the different phases of the sexual cycle in the rat. It was suggested that these variations might be related to feed-back processes associated with the regulation of the gonadotrophins secretion through the hypothalamic-hypophyseal system[9,10]. In our experiments, we observed that EB reproduced the effects of the estrogenic periods (proestrus, estrus, see Table II): a decrease of the NE/E relationship caused by the E increasing and the NE decreasing. P had the same effect as metaestrus (see Table II): a NE/E and NE increase; while TD did no alter the values observed in the oophorectomized animals. These results suggest the possibility that P stimulates the NE synthesis and/or a depletion from its deposits, while the estrogens tend to antagonize those effects. The results also seem to indicate that the estrogens increase the activity of the NE to E methylating enzyme, the phenoletanolamine-N-methyl transferase; the opposite of what would occur with P effects[11,12]. It must be pointed out that oophorectomy caused an elevation of E excretion as compared with the control animals. It seems possible that when the ovaries have been extracted, of all the secretions of the suprarenal sexual hormones, the estrogenic effects predominate over the progesteronic effects as far as the metabolism of the catecholamines is concerned. Another hypothesis suggests that, in the absence of the ovarian hormones, the effects of the 11 OH-corticosteroids of the adrenal cortex would be more evident. One has to recall that the 11 OH-corticosteroids (essentially the corticosterone, in the rat) are able to activate the phenoletanolamine-N- methyl transferase and to methylate the NE[13].

Resumen. Se estudió en ratas Wistar hembras, el efecto de la ovariectomía y la administración de estradiol, progesterona y testosterona, sobre la excreción urinaria de noradrenalina (NA), adrenalina (A) y al relación NA/A. La ovariectomía aumentó la excreción de A, disminuyendo la relación NA/A. El estradiol disminuyó la excreción de NA y la relación NA/A e incrementó la eliminación de A. La progesterona aumentó la excreción de NA, y la relación NA/A, la testosterona no modificó las catecolaminas urinarias.

A. E. DOMÍNGUEZ, N. A. VIDAL and B. E. FERNÁNDEZ

Departamento de Ciencias Biológicas, Orientación Fisiología Humana, Facultad de Farmacia y Bioquímica, U.B.A. Junín 956, Buenos Aires (República Argentina), 10 February 1975.

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