Effect of Adrenal Function on Level of Hepatic and Extrahepatic Arginase

It has been known for a long time that 17-OH steroids increase arginase activity in the liver[1-3]. It is also known that arginase activity in the liver is decreased in adrenalectomized animals[4,5]. Arginase activity in the liver is regulated not only by the corticoids but also by the dietetic factors[3]. 7 days of fasting produces a 3-fold increase of arginase activity in the liver, while a protein-free diet produces a decrease in the activity of this enzyme[3].

Arginase is, however, an enzyme widely distributed in animal tissues[6]. It is found in measurable quantities in the cells of numerous tissues, which do not participate in ureogenesis, and in the liver of vertebrates which do not excrete uric acid as the end product of nitrogen catabolism[6]. The role of this arginase is unknown. There is no information in the literature on the nature of factors which regulate the level of this extrahepatic (atypical) arginase.

The aim of the experiments described in this communication was to study the role of the adrenal gland in the regulation of renal arginase activity and to determine the level of sensitivity of renal arginase to hydrocortisone in comparison with hepatic arginase.

Material and methods. Experiments were done on male albino-rats of wistar strain (Vinča, Beograd), weighing about 120 g.

The animals were divided into 4 experimental groups. The first group of animals was given hydrocortisone acetate in a daily dose of 5 mg/100 g body wt. for 5 days. The second group received 10 mg/100 g body wt. daily for 5 days, and the third group was given 25 mg of hydrocortisone per 100 g body wt. also for 5 days. The control group of animals was given a corresponding amount of physiological saline. All the animals were sacrified 24 h after receiving the last dose of hydrocortisone. The animals from the fourth experimental group were adrenaloctomized. The operated animals were divided into 2 sub-groups. The first sub-group served as the control (II), and the second was treated with hydrocortisone in a daily dose of 10 mg/100 g body wt. for 5 days after the operation. The first injection was given 24 h after the operation. The animals were fed a balanced synthetic diet.

Arginase activity was determined in the liver and in the kidneys by the method of VAN SLYKE and ARCHIBALD[7]. The quantity of enzyme which produced 1 μmol of urea in 1 min, under standard conditions (38°C, pH = 8,6), was taken as the unit of arginase activity.

Results and discussion. It may be seen from the results shown in Table I that the effect of hydrocortisone administration on arginase activity in the liver depended on the dosage employed. Smaller doses of hydrocortisone (5 mg and 10 mg/100 g body wt.) had a weak effect on arginase activity in the liver, while higher doses of hydrocortisone (25 mg/100 g body wt.) changed significantly the activity of this enzyme in the liver. These results explain the earlier discrepancies concerning the effect of corticosteroids on arginase activity in the liver. The authors who used smaller doses of corticosteroids observed no change in the level of hepatic arginase[8], while those who used higher doses reported that corticoids increase the activity of this enzyme in the liver[9]. Adrenalectomy produces decrease of arginase activity in the liver (Table II), which is in accord with the findings of FOLLEY and GREENBAUM[4]. The effect of hydrocortisone administration on hepatic arginase was the same in adrenalectomized animals as in the intact ones (Tables I and II).

Unlike liver arginase, renal arginase was much more sensitive to exogenous hydrocortisone (Table I). Its activity increases 100% already after the injection of smaller doses of hydrocortisone (5 mg/100 g body wt.). The increase of the dose of hydrocortisone was associated with a proportional increase of arginase activity in the kidneys. Adrenalectomy, however, did not change the enzyme activity in the kidney. The effect of exogenous hydrocortisone on renal arginase was the same in adrenalectomized animals as in the intact ones (Table I).

The fact that renal arginase reacts already to smaller doses of hydrocortisone with a significant increase of activity, and that its activity remained unchanged after

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Table I. Effect of hydrocortisone on kidney and hepatic content of arginase

Experimental conditions	No. of animals	Arginase activity-units (M ± SD)	Increase (%)	Significance
Kidney				
Controls	7	9.68 ± 1.56	—	—
Hydrocortisone treated:				
5 mg/100 g body wt.	7	19.41 ± 2.67	+ 100.5	< 0.001
10 mg/100 g body wt.	7	24.48 ± 4.20	+ 152.9	< 0.001
25 mg/100 g body wt.	7	31.44 ± 2.37	+ 224.8	< 0.001
Liver				
Controls	7	308.7 ± 41.4	—	—
Hydrocortisone treated:				
5 mg/100 g body wt.	7	361.0 ± 60.0	+ 11.7	> 0.05
10 mg/100 g body wt.	7	356.0 ± 41.3	+ 15.3	> 0.05
25 mg/100 g body wt.	7	795.9 ± 10.9	+ 157.8	< 0.001

Table II. Effect of adrenalectomy on the activity of kidney and liver arginase

Experimental conditions	No. of animals	Arginase activity-units (M ± SD)	Difference (%)	Significance
Kidney				
Controls (I)	7	9.86 ± 1.56	—	—
Adrenalectomy (control II)	7	11.85 ± 1.28	+ 22.46	> 0.05
Adrenalectomy + hydrocortisone 10 mg/100 g body wt.	7	26.33 ± 2.52	+ 163.86	< 0.001
Liver				
Controls (I)	7	308.7 ± 41.4	—	—
Adrenalectomy (control II)	7	206.3 ± 85.0	— 33.0	< 0.01
Adrenalectomy + hydrocortisone 10 mg/100 g body wt.	7	375.1 ± 48.0	+ 21.59 (Con. I) + 81.70 (Con. II)	> 0.05 < 0.01

adrenalectomy (in contrast to hepatic arginase) can be used as the material basis for the idea that arginase activity in the kidney and in the liver is regulated in a different way. The finding that arginase in the kidneys remained unchanged after adrenalectomy introduces the question whether corticosteroids have any direct influence at all on the regulation of the activity of this enzyme in the kidney. The increase in arginase activity under the influence of exogenous hydrocortisone may be secondary in nature, namely it may be in close association with the increased excretion of the products of protein catabolism.

Résumé. On a constaté que l'arginase des reins est plus sensible que l'arginase du foie a l'hydrocortisone injecté. Au contraire, l'adrénalectomie provoque la réduction de l'activité arginasique du foie mais ne modifie pas le niveau de l'arginase rénale.

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Inhibition of Ovarian Compensatory Hypertrophy by Water Deprivation[1]

The establishment of an anoestrous condition in the rat by prolonged water depletion[2] suggests that this procedure induces inhibition of estrogenic secretion by the ovary in spite of the observed increase both in production and release of gonadotrophin[3].

It is known that hemicastration in rats produces ovarian hypertrophy as a result of increased gonadotrophic activity[4] and that water deprivation causes no changes in ovarian weight[2]. We produced water deprivation in rats to study its inhibitory action on ovarian compensatory hypertrophy.

The experiments were carried out in 20 female adult albino rats of our stock weighing between 105 and 233 g and having had at least 3 regular 4–5-day estral cycles. The animals were kept on a 14-h light and 10-h dark schedule. The rats were randomly divided into 2 groups: 1. control water deprived (CWD) and 2. hemicastrated and then water deprived (HWD).

Hemicastration was accomplished by the lumbar route under pentobarbital anesthesia (33 mg/kg body wt.). The excized ovaries were used to control the weight of the remaining ovary in each animal. In a previous experiment bilateral ovariectomy was performed in 26 rats, and both ovaries' weights were compared by the Student's test for paired data. The mean difference was 0.77 mg ± 0.98 SE ($t = 0.78$ NS). 48 h after hemicastration both groups were deprived of water; a standard dry diet for rats (13% water content) was given ad libitum. Vaginal smears and body weight were both controlled daily. The rats were killed under pentobarbital anesthesia when their weight loss had reached 40% of the initial body weight; i.e. after an average of 12.3 ± 0.3 and 11.5 ± 0.4 days in the (CWD) and (HWD) groups respectively.

The ovaries were carefully dissected and weighed on a Monopan balance (0.05 mg precision). They were fixed in 10% formalin for routine histologic techniques and examination.

The vaginal smear showed a continuous di-oestrous during the whole water deprivation period in both groups.

Histologic studies showed that in the ovaries of the water deprived rats there is a decrease in the number of large follicles with an increase in atresia. No changes were observed in the number of corpora lutea. Thus, in the ovaries of the water deprived animals there is an increase in the relation corpora lutea-normal follicles. A decrease in the ovarian stroma was also observed. 2 types of abnormalities were observed in the interstitial cells of the ovaries. Some cells were sphere-shaped and of a larger than normal size, their cytoplasm filled with vacuoles (xanthomatous appearance). These sphere-shaped cells

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