of splenic contraction (haemoconcentration), are not the result of it.

Since both GOT and LDH have relatively short plasma halflives ($t_{1/2}$), whatever promotes their increase early in stimulation must continue until stimulation ceases[4,5]. The time course suggests a rapid step alteration in either the introduction (an increase) and/or the clearance (a reduction) of both enzymes within the plasma compartment upon commencing stimulation. Enzyme clearance is accomplished by several mechanisms[6]. One of these, uptake by the reticulo-endothelial system (RES), is known to clear both GOT and LDH from the extracellular fluid[5]. Since this clearance occurs primarily in the hepatic and splanchnic vascular beds it is conceivable that a reduction in the blood flow through these beds would result in a reduction in plasma enzyme clearance. Such a mechanism may have occurred during muscle stimulation. The degree of splanchnic vascular constriction and splenic contraction would likely be similar since they are both responses to increases in sympathetic activity. Further, the $t_{1/2}$s of GOT and LDH may be sufficiently short to account entirely for the muscle stimulation induced increases in the plasma levels of these 2 enzymes purely through a reduction in the rate of their clearance from the plasma. Data obtained in the dog have indicated a plasma $t_{1/2}$ of approximately 30 min for both the muscle-type and heart-type isoenzymes of LDH[5]. Estimates of the plasma $t_{1/2}$ for the mitochondrial and cytoplasmic isoenzymes of GOT in the dog have yielded values of 54 min and 4.0 h, respectively[4,7].

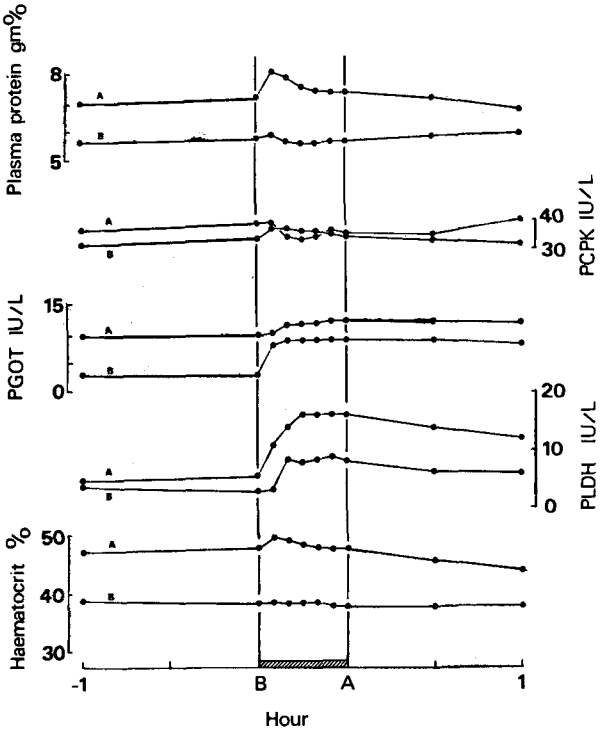

Fig. 3. Changes in plasma enzyme activity, arterial haematocrit, and plasma protein concentration during 30 min of stimulation ($N = 2$) following acute splenectomy.

On the basis of these observations we suggest that one mechanism involved in the plasma enzyme response to exercise is a reduction in the clearance of enzyme from the extracellular fluid in the face of either a normal or increased entry of enzyme into this compartment. One explanation of the reduction in the plasma enzyme response to exercise seen following physical training would therefore invoke a change in the distribution of blood blow during exercise in the trained individual. Such changes have been demonstrated and support this hypothesis[8].

[4] K. G. WAKIM and G. A. FLEISHER, J. Lab. clin. Med. *61*, 86 (1963).
[5] K. G. WAKIM and G. A. FLEISHER, J. Lab. clin. Med. *61*, 107 (1963).
[6] S. POSEN, Clin. Chem. *16*, 71 (1970).
[7] G. A. FLEISHER and K. G. WAKIM, J. Lab. clin. Med. *61*, 98 (1963).
[8] L. B. ROWELL, J. R. BLACKMAN and R. A. BRUCE, J. clin. Invest. *43*, 1677 (1964).

On the Role of the Decreased Renal Vascular Resistance in the Mechanism of Volume Natriuresis

B. LICHARDUS, J. PONEC and R. TUREK[1]

Institute of Experimental Endocrinology, Slovak Academy of Sciences, Vlarska 3, CS-809 36 Bratislava-Kamáre (Czechoslovakia), 15 December 1975.

Summary. Acute hypohysectomy (AH) prevented the increase of the cardiac output, renal cortical blood flow (e.g. the decrease of the renal vascular resistance) and renal sodium excretion during the ECFV expansion. The non-occurrence of natriuresis in AH rats is suggested as being partly in causal relation to the inability to decrease the renal vascular resistance and thus to incrase the peritubular hydrostatic pressure.

Much effort has been concentrated on exploring a possibility of the existence of a humoral inhibitor of the sodium tubular transport, since DE WARDENER's et al.[2] evidence on the tubular nature of natriuresis due to the expansion of the extracellular fluid volume (ECFV) with saline ('saline' or 'volume' natriuresis). The prospective hormone has been called the 3rd factor or a natriuretic hormone[3,4]. However, it was latter found that volume natiuresis in dogs was accompanied by the increased renal blood flow even if the kidney was not connected with the organism by nerves and the blood perfusion pressure was constant[5]. So it was suggested that besides a humoral inhibitor of the sodium tubular transport also a vasodilatory humoral substance might circulate in plasma of dogs with the increased ECFV[5]. An alternative possibility is that a vasoconstrictory agent in plasma may disappear. The resulting vasodilation might then contribute to the inhibition of sodium transport as well. The results of the present experiments are considered to be consistent with these previous suggestions concerning the mechanism of volume natriuresis.

Material and methods. 54 male Wistar rats (Institute of Experimental Endocrinology, Slovak Academy of Sciences SPF breeding) were anaesthetized by Inactin Promonta, then the trachea was cannulated and in 24 rats an acute hypophysectomy was performed by parapharyn-

The effect of extracellular fluid volume expansion (EXP) with isotonic saline in controls (sham-hypophysectomized) and in acutely hypophysectomized (HYPOX) anaesthetized rats

I Controls ($n = 14$)	II Controls EXP ($n = 16$)	III HYPOX ($n = 12$)	IV HYPOX EXP ($n = 12$)	Significance ($P <$)			
				I:II	I:III	II:IV	III:IV
BP torr							
130.21 ± 2.26	117.69 ± 2.15	116.00 ± 3.73	115.42 ± 4.44	0.001	0.01	ns	ns
CO							
28.91 ± 2.04	44.26 ± 3.52	27.47 ± 1.98	30.48 ± 2.48	0.002	ns	0.01	ns
RCBF							
11.20 ± 0.92	16.09 ± 1.49	10.03 ± 1.00	9.60 ± 0.76	0.02	ns	0.001	ns
$U_{Na}V$							
$n = 13$	$n = 13$	$n = 13$	$n = 11$				
0.09 ± 0.02	6.28 ± 0.59	0.03 ± 0.01	1.06 ± 0.25	0.001	0.05	0.001	0.02

The means + SE of the following parameters are represented: BP, arterial blood pressure; CO, cardiac output calculated per 100 g of the body weight; RCBF, renal cortical blood flow per 1 g of the cortical tissue weight; $U_{Na}V$, renal sodium excretion per 1 g of the kidney weight.

geal path. The surgical preparation in all rats was completed by cannulating carotid artery, jugular vein, femoral artery and urinary bladder with polyethylene catheters. Finally the animals were heparinized. Following the surgical preparation, the rats rested for 1 h on a heated table. The experiments in all animals, divided into 4 experimental series, started by a 20 min control urine sampling period. In 14 controls (series I) and in 12 acutely hypophysectomized rats (series III), mean arterial blood pressure (BP) was continuously monitored by a polygraph, cardiac output and renal cortical blood flow (RCBF) were measured by means of ^{86}Rb under the conditions of the normal, e.g. unexpanded, ECFV. The rats were sacrified thereafter. In another series of 16 rats (series II) and in 12 acutely hypophysectomized rats (series IV), the same parameters were measured following an i.v. infusion of isotonic saline applied immediately after the control urine sampling period in 2 subsequent 20 min periods in the total amount of 6% of the body weight. Renal sodium excretion ($U_{Na}V$) was determined by flame photometry in another 4 series of 50 rats treated exactly according to the same 4 types experimental protocols. The results were statistically analyzed by the Student *t*-test by using an optimalized programme for electronic computer Olivetti Programma 101 and 203[6].

Results and discussion. The ECFV expansion with saline in control animals decreased the mean arterial blood pressure and increased cardiac output, renal cortical blood flow and renal sodium excretion (I:II). Acute hypophysectomy also decreased blood pressure in comparison with control unexpanded animals (I:III), and the ECFV expansion did not further change it (III:IV). Cardiac output and renal cortical blood flow also remained unchanged (III:IV). The renal sodium excretion increase in the control rats following saline infusion was 6 times more pronounced than in the hypophysectomized animals (II:IV).

We have as yet no direct data on the state of the active tubular transport in these types of experiments. However, if the renal blood perfusion pressure during the ECFV expansion is the same in both the control and acutely hypophysectomized rats (II:IV), and the renal vascular resistance decreases only in the controls (II), then the increase of the peritubular vascular hydrostatic pressure is expected to be more pronounnced in the control rats (II). It was shown by others that the increase of the peritubular vascular hydrostatic pressure is a major physical natriuretic factor in the mechanism of volume natriuresis[7]. So it seems probable that the failure to develop a homeostatically effective saline natriuresis in acutely hypophysectomized rats could be at least partly in causal correlation with the inability to increase the cardiac output and the renal cortical blood flow, e.g. to decrease the renal vascular resistance[8,9]. The latter could be a result of the generally decreased adrenergic activity due to the cardio-renal reflex[10], and/or of a direct effect of a more specific pituitary factor on the renal mechanisms regulating the renal vascular tone. It has not been established as yet with certainty which pituitary factor is involved, but neither the pituitary-adrenal[11,12] nor the pituitary-thyroid axis[12] are likely to be. It has also been previously suggested that it is rather the posterior pituitary hormones[8,13,14] than the anterior pituitary ones which play a role in the mechanism of saline natriuresis.

[1] Expert technical assistance of Mrs. E. Blašková, J. Kyselicová and Mr. Š. Kaločai is sincerely acknowledged.

[2] H. E. De Wardener, I. H. Mills, F. W. Clapham and J. C. Hayter, Clin. Sci. *21*, 249 (1961).
[3] J. H. Cort and B. Lichardus, Nephron *5*, 401 (1968).
[4] H. E. De Wardener, in *Dialysis, Transplantation, Nephrology*. Proc. 10th Congr. EDTA Vienna 1973 (Ed. J. F. Morhead; Pitman Medical, New York 1974), p. 3.
[5] B. Lichardus and J. W. Pearce, Nature, Lond. *209*, 407 (1966).
[6] M. Mikulecký and A. Bezák, Research Report (Faculty Hospital, Bratislava 1971).
[7] F. G. Knox, E. G. Schneider, L. R. Willis, J. W. Strandhoy, C. E. Ott, J. L. Cuche, R. S. Goldsmith and C. D. Arnaud, J. clin. Invest. *53*, 501 (1974).
[8] B. Lichardus, J. Ponec and I. Albrecht, in *Endocrinology*. Proc. 4th int. Congr. Endocrin., Washington DC 1972 (Ed. R. O. Scow; Excerpta Medica, Amsterdam 1973).
[9] B. Lichardus, J. Ponec and R. Turek, 2nd int. Congr. Pathophysiol, Praha 1975, Abstracta No. 230.
[10] B. Lichardus, Endocrinologia exp. *1*, 181 (1967).
[11] A. T. Veress and J. W. Pearce, Proc. Soc. etp. Biol. Med. *145*, 533 (1974).
[12] J. Ponec, V. Štrbák, M. Alexandrová and B. Lichardus, Physiol. bohemoslov., in press.
[13] R. C. De Bodo, I. L. Schwartz, J. Greenberg, M. Kurtz, D. P. Earley and S. J. Farber, Proc. Soc. exp. Biol. Med. *76*, 612 (1951).
[14] T. W. Demunbrun, A. D. Keller, A. H. Levkoff, R. M. Purser, Am. J. Physiol. *179*, 429 (1954).