excitation into the ganglia, by playing the role of modulators [5]. Which explanation is more in accordance with reality only closer investigations carried out for this purpose will show.

Neurons of the myenteric plexus in segments of the large intestine lying in the zone of innervation of the caudal mesenteric sympathetic ganglion, the cells of which have a regulatory effect on contractions of its distal part [1], were found to be most sensitive to A and NA. In this connection, neurons of the intramural ganglia in this region, it can be suggested, are more vulnerable to the influence of sympathetic postganglionic fibers than cells of the plexuses of the small intestine.

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CHANGES IN THE SYSTEMIC HEMODYNAMICS PRODUCED BY VASOPRESSIN IN DOGS DURING INDIVIDUAL DEVELOPMENT

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Indices of the central hemodynamics were studied in puppies aged 18-22 days and 2-3 months and in dogs aged 3-5 years after intravenous injection of synthetic vasopressin (0.8 unit/kg body weight). The pressor effect was strongest in the adult dogs and bradycardia in the puppies aged 18-22 days. The cardiac output was reduced in all animals and the peripheral resistance considerably increased. In adult dogs the external work of the left ventricle and the energy consumption of the heart were increased. In puppies a reduction in the volume velocity of ejection of blood and in the external work of the heart was combined with a smaller increase in energy consumption.

KEY WORDS: *systemic hemodynamics; vasopressin; individual development.*

Activation of hypothalamic neurosecretion and mobilization of neurohormones into the bloodstream are observed in response to the action of various stressors. Oxytocin and vasopressin, on entering the circulation, bring about various adaptive responses of the body. Meanwhile, many investigations [2, 5, 6, 8, 11-13, 20, 22] have shown that a similar response of the neurosecretory system is observed during the development of experimental hypertension and of essential hypertension in man. It is generally accepted that the neurohormones mobilized into the blood stream in these cases are implicated in the genesis of the pathological process and that they can cause the specific changes of hypertension. One method of studying the possible role of these hormones in the circulatory changes of hypertension is by the analysis of their intrinsic hemodynamic effects. The effect of vasopressin on indices of

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TABLE 1. Changes in Indices of Systemic Hemodynamics following Administration of Vasopressin to Dogs of Different Ages

Index	Initial level	Vasopressin	20 min later
	Puppies aged 18-22 days		
BP, mm Hg	97,43±3,34	131,00±4,02*	100,00±3,74
Heart rate, beats/min	204,00±9,02	116,13±6,43*	155,00±9,50*
TPR, dynes·sec·cm^{-5}	32736,90±836,06	82492,42±6703,26*	40672,60±1009,78*
Cardiac index, liters/m^2	2,51±0,02	1,31±0,08*	2,03±0,06*
Systolic index, ml/m^2	12,34±0,54	12,66±0,84	13,14±0,67
WILV, kg·m/m^2	3,38±0,07	2,30±0,12*	2,83±0,10*
WSILV, g·m/m^2	16,39±0,93	27,71±1,30*	18,01±0,65
P, W	0,19±0,005	0,21±0,02	0,17±0,01
	Puppies aged 2-3 months		
BP, mm Hg	113,60±3,81	156,00±8,02*	118,33±3,11
Heart rate, beats/min	135,20±2,66	86,83±6,10*	106,60±4,21*
TPR, dynes·sec·cm^{-5}	26723,10±1162,24	61405,52±1078,88*	39966,32±2654,54*
Cardiac index, liters/m^2	1,01±0,03	0,64±0,01*	0,70±0,02*
Systolic index, ml/m^2	7,49±0,25	6,78±0,24	6,82±0,34
WILV, kg·m/m^2	1,58±0,08	1,27±0,06*	1,11±0,03*
WSILV, g·m/m^2	12,26±0,63	14,56±0,50*	10,60±0,38*
P, W	0,45±0,02	0,37±0,04*	0,32±0,01*
	Adult dogs aged 3-5 years		
BP, mm Hg	169,00±4,26	246,66±3,74*	175,00±5,60
Heart rate, beats/min	82,33±1,67	59,33±2,11*	74,33±1,31*
TPR, dynes·sec·cm^{-5}	5682,01±249,08	11051,94±253,89*	6829,08±251,53*
Cardiac index, liters/m^2	1,57±0,03	1,18±0,04*	1,36±0,04*
Systolic index, ml/m^2	19,20±0,55	20,31±0,74	18,40±0,73
WILV, kg·m/m^2	3,60±0,15	3,88±0,10	3,20±0,19
WSILV, g·m/m^2	45,07±3,16	66,50±2,88*	42,94±3,03
P, W	4,82±0,06	9,54±0,45*	5,16±0,06*

*P < 0.05.

hemocirculatory homeostasis has frequently been studied [4, 16, 17, 19, 21]. Meanwhile, no reports of investigations of age differences in the hemodynamic changes in response to the action of vasopressin could be found in the literature with the exception of studies of old animals [4, 16].

The present investigation was accordingly carried out in order to study changes in the principal hemodynamic indices in puppies and dogs in response to the action of exogenous vasopressin.

EXPERIMENTAL METHOD

Unanesthetized puppies aged 18-22 days and 2-3 months and adult dogs aged 3-5 years (6 males in each case) were used. Synthetic vasopressin free from oxytocin (Koch-Light Laboratories Ltd.) was injected through a Teflon catheter into the femoral vein in a dose of 0.8 unit/kg body weight. Preliminary investigations showed that smaller doses of vasopressin gave rise to only an inconstant and weak pressor effect in puppies. The blood pressure (BP) in the femoral artery was recorded by a mercury manometer. The cardiac output (CO) and systolic volume (SV) were determined by the thermodilution method [7] with synchronous recording of the ECG in lead II. The polycardiograms were recorded on the 6-NÉK-3 electrocardiogram. The total peripheral resistance (TPR), cardiac and systolic indices, external work of the heart, volume velocity of ejection of blood by the left ventricle, and power of the myocardium of the left ventricle (P) were calculated. The work index of the left ventricle (WILV) was calculated by the equation WILV = BP × cardiac index × 0.0136 kg·m/m^2; the work stroke index of the left ventricle (WSILV) by the equation: WSILV = BP × systolic index × 0.0136 g·m/m^2; and the energy consumption per liter cardiac output by the ratio:

$$P \times \frac{\text{ejection time of cardiac output}}{\text{cardiac output}}$$

and expressed in W·sec/liter.

The tests were carried out in the initial state, at the height of the pressor effect of vasopressin, and 20 min after its injection. The results were subjected to statistical analysis by computer with the use of Peters' constant.

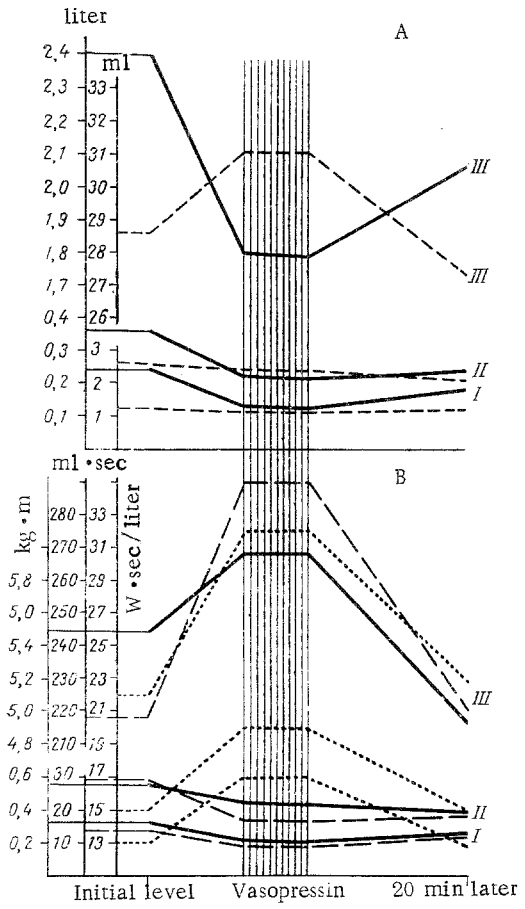

Fig. 1. Changes in cardiac activity after administration of vasopressin to dogs of different ages. A: Continuous lines show cardiac output, broken lines systolic volume. B: Continuous lines show external work of left ventricle, broken lines volume velocity of blood ejection, dotted lines energy expenditure per liter cardiac output. I) Puppies aged 18-22 days; II) puppies aged 2-3 months; III) adult dogs.

EXPERIMENTAL RESULTS

The pressor effect of vasopressin was maximal in all the animals 1-2 min after injection of the hormone, but it was most marked in the adult dogs (Table 1). At the height of hypertension, bradycardia was observed; the minimal hypertensive response in the puppies aged 18-22 days was accompanied by the most marked decrease in the heart rate.

The increase in BP in all the animals took place on account of a sharp increase in the TPR. The cardiac output and, correspondingly, the cardiac index were substantially reduced. In the animals of all age groups the decrease in cardiac output was not accompanied by any significant change in the systolic index; in the sexually mature dogs, however, the decrease in cardiac output was accompanied by a tendency toward an increase in systolic volume (Fig. 1A). In the adult animals there was a corresponding increase in the external work of the heart, the volume velocity of blood ejection, and the expenditure of energy per liter of cardiac output (Fig. 1B). In the puppies of both age groups the volume velocity of ejection and the external work of the heart were reduced but the increase in the expenditure of energy was not so marked, especially in the puppies aged 18-22 days. Consequently, the less marked slowing of the heartbeat coupled with the tendency toward an increase in systolic volume led to an increase in the external work of the heart in the adult dogs. The power of the left ventricle was doubled in this group. The peripheral vasoconstrictor effect of vasopressin in the adult animals, despite the decrease in cardiac output, was thus combined with an increase in the work of the left ventricle. An increase in WSILV also was observed in the puppies but the considerable bradycardia led to a significant decrease in the external work of the heart.

In all the animals 20 min after injection of vasopressin BP was close to its initial level but TPR remained significantly higher and the cardiac output lower than initially.

The decrease in cardiac output in all the animals in response to injection of vasopressin probably took place not only through an increase in the resistance to injection of the blood, but also in connection with the well-known [14] spastic effect of the hormone on the coronary circulation. The more severe bradycardia in the puppies was evidently attributable not only to a baroreceptor reflex, but also to a response of the heart to the myocardial hy-

poxia arising under the influence of vasopressin, for we know [1, 9, 10] that in early development hypoxia leads to a slowing of the heartbeat. In adult dogs reflex bradycardia is evidently limited by the increased heart rate caused by hypoxia. The myocardium of puppies is less sensitive to hypoxia [1, 9, 10] and, in accordance with the results of the present investigation, the expenditure of energy by the heart rises less substantially after injection of vasopressin in puppies than in adult animals. After administration of exogenous vasopressin more unfavorable conditions for cardiac function are thus created in adult dogs.

The lower intensity of the pressor response in puppies perhaps reflects a lower sensitivity to vasopressin than in adult dogs. Similar results were obtained when the pressor effect of vasopressin was compared in young and adult rats [18]. The writers showed previously [3] that activation of neurosecretion of the supraoptic nuclei of the hypothalamus during stress in puppies is much weaker than in adult dogs. The low level of activity of the system in early ontogeny was evidently combined with lower sensitivity to neurohormones. This view is in agreement with the results of investigations by Frol'kis [15], who showed that the sensitivity of the cardiovascular system to humoral influences increases with age.

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