PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

FUNCTION OF THE ADENOHYPOPHYSIS AND ADRENAL CORTEX IN EXPERIMENTAL TRAUMATIC SHOCK

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Although many investigators have shown interest in the endocrine changes occurring in response to trauma and surgical operations [10-12,14], inadequate study has been made of the state of the pituitary–adrenal system (PAS) in traumatic shock. For a long time, the pathogenesis of shock was associated with the exhaustion of the adrenal cortex and with the development of adrenocortical failure following overstrain [1,9,18,21,22]. This theory was supported by the fact that in hypophysectomized and adrenalectomized animals, there is no adequate metabolic reaction to trauma or surgical operation, and they die quickly with signs of shock [1,21,22].

Patients with chronic adrenocortical failure develop irreversible shock even in the course of minor operations. The operative mortality among patients with Addison's disease is 56% [6].

Administration of adrenocortical extracts and steroid hormones to adrenalectomized and healthy animals increases their resistance to trauma [2,23]. Some of the symptoms forming the clinical picture of traumatic shock (hypothermia, hypotension) resemble those of chronic adrenal cortical failure [1].

On the basis of the theory of exhaustion of the adrenal cortex in traumatic shock which was deduced from these observations, many authors have described the use of steroid hormones and ACTH (with conflicting results) along with other measures in the treatment of shock arising in such patients [5,8]. More recent publications have contradicted this theory of the pathogenesis of shock.

Following acute blood loss in dogs, the level of 17-hydroxycorticosteroids and ACTH in the peripheral blood is elevated in the period of hypotension [13]. Reports have also been published [7,8,20] of an increase in the 17-hydroxycorticosteroid (17-HCS) concentration in the plasma of persons in a state of traumatic shock.

Because the state of the PAS in the various periods of traumatic shock has not yet been studied either clinically or experimentally, the present investigation was carried out for this purpose, using the method of parallel determination of the free 17-HCS and ACTH in the blood plasma.

EXPERIMENTAL METHOD

The investigation was carried out on dogs of both sexes, weighing 9-23 kg, and on male albino rats weighing 100-340 g. Shock was produced in the dogs by crushing the soft tissues of the thigh with a heavy weight. The number of blows applied varied from 50 to 320 (mean 240). Trauma was accompanied by a fall of arterial pressure, on the average to 70 mm, and by the appearance of signs of shock.

The concentrations of ACTH and 17-HCS were investigated in the plasma of venous blood obtained before trauma, immediately after trauma (which lasted 9-37 min), and in the torpid phase of shock, 48-210 min after trauma (at the beginning of the agonal period). The total blood loss as a result of taking blood samples for investigation averaged 200 ml (0.9-2.5% of the body weight). The blood pressure in the right carotid artery was recorded by means of a mercury manometer, and respiration by means of a cuff placed around the animal's chest and connected

Concentration of ACTH in Blood Plasma (in mg% Lowering of Ascorbic Acid Concentration in Adrenals of Rats) and of 17-HCS in Plasma of Dogs with Traumatic Shock

Group of animals	Experiment No.	Weight (in kg.)	After fixation				Erectile phase				Torpid phase			
			Number of rats	Difference in ascorbic acid concentration (in mg%)	17-HCS (in μg%)	Time after beginning of trauma (in min)	Number of rats	Difference in ascorbic acid concentration (in mg%)	17-HCS (in μg%)	Time after beginning of trauma (in min)	Number of rats	Difference in ascorbic acid concentration (in mg%)	17-HCS (in μg%)
1-	2	21,0	3	— 18	16,6	20	3	— 24	20,0	145	4	— 59	28,5
	3	19,0	4	— 7	0,9	17	4	+ 7	20,0	109	3	— 28	20,0
	4	17,3	3	— 7	10,6	21	4	+ 15	60,0	154	4	— 108	40,0
	6	17,3	4	— 63	24,0	27	2	— 132	15,0	90	4	— 58	28,0
	9	9,0	4	— 9	20,0	25	2	+ 44	24,1	128	4	— 52	40,0
	10	17,2	2	— 9	16,0	20	4	— 17	19,5	210	4	— 51	28,0
	12	10,9	4	— 50	24,0	—	—	—	22,0	83	4	— 72	16,0
	13	11,4	4	— 46	29,3	24	4	— 3	20,4	90	3	— 54	19,8*
	14	18,8	3	— 42	19,3	20	4	— 19	22,3	67	4	— 94	22,5*
	$M \pm m$	15,8		$-30 \pm 10,6$	$17,8 \pm 3,3$			$-11 \pm 12,2$	$24,8 \pm 5,3$			$-64 \pm 9,86$ $P_{1-3} < 0,01$	$27 \pm 2,8$ $P_{1-3} < 0,05$
2-	1	23,0	3	— 70	30,4	20	3	— 40	18	35	4	+ 30	26
	5	16,1	4	— 25	4,0	9	4	— 59	30	93	3	— 32	30
	7	13,4	4	— 30	25,0	37	4	— 16	31	63	4	— 9	17,2
	8	12,2	4	— 50	10,9	13	4	— 14	27,2	48	4	— 26	66,5
	15	17,1	4	+ 38	28,7	14	3	— 18	28,8	129	4	— 1	34,8
	$M \pm m$	16,3		$-26,5 \pm 12,5$	$19,8 \pm 5,6$			$-29,0 \pm 18,45$ $P_{1-2} > 0,05$	$27,0 \pm 2,6$ $P_{1-2} > 0,05$			$-14 \pm 15,37$ $P_{1-3} < 0,05$	$24,9 \pm 3,9$ $P_{1-3} < 0,05$

* Determination immediately after death of animal.

to a Marey's tambour. The adrenocorticotropic activity of the plasma was determined by Sayers' method [19], based on the ability of ACTH to lower the ascorbic acid level in the adrenals of rats. The concentration of the latter was estimated by the method of Roe and Kuether [17]. The effect of endogenous ACTH on the adrenals of the rats was abolished by intraperitoneal injection of cortisone [4] or of hydrocortisone 4 h before the experiment [16]. The concentration of 17-HCS in the plasma was determined by the method of Silber and Porter, as modified by N. A. Yudaev and Yu. A. Pankov [15]. The hypophysis and adrenals of the dying animals were investigated histologically.

The present report describes the results of experiments on 15 dogs and 178 rats. One dog, killed by massive exsanguination, was used as a control for the histological investigations of the pituitary and adrenals.

EXPERIMENTAL RESULTS

The fixation and subsequent injury of the animals evoked generalized excitation and raised the arterial pressure from 112-170 mm (mean 130) to 130-224 mm (mean 164). The pattern of the subsequent course of the shock was such that the dogs could be subdivided into two groups, differing with respect to their length of survival and the dynamics of the concentration of hormones in the blood. In the nine animals of group 1, the arterial pressure fell actually during trauma on the average to 77 mm, and a deep depression developed so that the animals did not react to trauma. The mean number of blows required to produce shock in this group was 194. In group 2, although the arterial pressure fell to 57 mm, the five dogs remained restless, with marked motor excitation which continued until death. To produce shock in the animals of this group, 146 blows had to be applied.

The results of the investigation of the adrenocortical activity and of the 17-HCS concentration in the plasma are given in the table.

Fixation, and dissection of the blood vessels, stimulated the adenohypophysis and the adrenal cortex of the unanesthetized animals, so that the initial concentration of 17-HCS in the plasma was higher than in the healthy dogs (1.0-3.3 μg%). At the same time, in 8 of the 14 animals, a high concentration of ACTH was found, whereas in healthy dogs [16] or humans [3] at rest no ACTH could be detected by Sayers' method.

In the erectile stage of shock in the animals of both groups, a further increase in the concentration of 17-HCS above the initial level was observed. The ACTH concentration was very slightly increased in the group with marked excitation, while in the animals with depression it was lowered to a level lying below the limit of sensitivity of the method. It may be assumed that the change in the secretion of ACTH in the erectile phase was determined, in the first case, by the stimulating influence, and in the second case by the inhibitory influence, of the hypothalamus on the adenohypophysis. This suggestion is in agreement with observations [2] showing that, in traumatic shock, inhibition spreads to the subcortical centers. Depression of the function of the adenohypophysis is evidently one of the manifestations of inhibition of the brain stem.

In the animals of group 1 in the torpid phase of shock (with marked depression), the concentrations of ACTH and 17-HCS in the blood plasma were considerably raised. In the dogs of group 2 (with increased excitation) in this phase the level of ACTH in the plasma was considerably lowered, while the concentration of 17-HCS was lowered by a lesser degree. The difference between the ACTH concentrations in the plasma of the two groups of animals is statistically significant ($P < 0.02$).

These results demonstrate a parallel trend between the severity of the traumatic shock and the concentration of ACTH and of 17-HCS in the blood plasma. In fact, in the dogs with a higher level of these hormones in the blood, the duration of survival was longer (125 min) than in the case of the animals of the other group (76 min) ($P < 0.05$).

Histological investigation of the adrenal cortex of the dogs which had died, using sections stained with hematoxylin and eosin, revealed slight infiltration of the adrenal cortex of some of the animals with leukocytes; in sections stained with Sudan III from three dogs, the lipid content was reduced.

The results obtained do not confirm the view that exhaustion of the function of the adenohypophysis and adrenal cortex develops in the course of brief (less than 3.5 h) traumatic shock. The increase in the concentration of 17-HCS in the plasma of the peripheral blood, persisting until the animals' death, is evidence of intensified functional activity of the adrenal cortex. The two types of change in the ACTH concentration in traumatic shock, corresponding to differences in the character of the reaction of the animals' nervous system, point to the influence of the central nervous system on the function of the adenohypophysis.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**
