THE ROLE OF THE PITUITARY-ADRENAL SYSTEM IN THE RESTORATION OF THE VITAL FUNCTIONS AFTER CLINICAL DEATH*

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Disorders in the central nervous system play a decisive role in the pathogenesis of terminal states which include death due to haemorrhage. The high sensitivity of the nervous system to lack of oxygen determines the duration of the clinical death as well as the possibility and the success of resuscitation [14, 15]. At the same time the normal function of the peripherical organs and effector systems represents a prerequisite for successful resuscitation, as functional disorders of these systems renders resuscitation more difficult. From this point of view the endocrine glands which by means of their hormones take part in the body's defense reactions occupy a particular place [4, 16].

Loss of blood, trauma and many other pathogenic factors cause, as shown by the investigations of Selye and other authors, a mobilization of anterior pituitary hormones and of hormones of the adrenal cortex [25, 26]. Adrenal failure enchances the development of shock and collapse [2, 12, 21, 26].

The role of the pituitary-adrenal system in the restoration of the vital functions after clinical death has not been adequately discussed in the literature. It has been shown in the laboratory of V. A. Negovskii that adrenalectomized animals can be revived and the special features characterizing their metabolic disorders were studied [3]. The investigations of the author carried out jointly with M. G. Polyakov and G. S. Yakobson established that revival of adrenalectomized animals after fatal haemorrhage is difficult and the more so the higher the degree of adrenal failure [8].

In the present paper we studied the influence exerted by the loss of function of the anterior pituitary lobe upon revival after clinical death caused by haemorrhage.

METHOD

The experiments were carried out on cats of both sexes. The hypophysectomy was carried out under participation of the assistant V. I. Fedenkov by a slightly modified method from that described in the literature [6, 7, 9]. The pituitary gland was removed under intratracheal narcosis through the oral cavity. As a reference point for the trepanation of the skull basis a canal in the bone was used which contained blood vessels and the rudimentary cranio-pharyngeal duct which leads from the pharynx to the pituitary gland. This canal is situated in the middle of a line which unites the basis of the left and right pterygoid process of the mandible and appears after dissection and separation of the mucous membrane and the periosteum in the shape of a punctiform opening in

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TABLE 1
Features Characterizing the Process of Dying and Resuscitation

Experimental series	No. of exp.	Duration			Time of restoration of the cornea reflexes	
		of the dying process	of clinical death	of respiration	counted from the reappearance of breathing	counted from the beginning of resuscitation
Hypophysectomized animals	1	45 min 40 sec	4 min 50 sec	3 min	16 min	19 min
	2	34 min	5 min 30 »	19 min 20 sec	17 »	36 » 20 sec
	3	46 min 40 sec	5 » 30 »	27 » 40 »	26 »	53 min 40 »
	4	45 »	5 » 30 »	6 » 30 »	16 »	24 » 30 »
	5	34 min	5 » 35 »	5 »	17 »	22 »
	6	34 » 50 sec	5 » 30 »	3 min 20 sec	16 »	19 min 20 sec
	7	29 min	4 min 55 »	2 » 35 »	16 »	18 » 35 »
	8	35 » 30 sec	5 min 05 »	3 » 25 »	12 »	15 » 25 »
	9	48 »	6 »	3 » 20 »	19 »	22 min 20 »
	10	47 » 45 sec	6 »	5 min 30 »	17 » 30 sec	23 min
Control animals	*M*	40 min 03 sec	5 mins 22 sec	7 min 57 sec	17 min 13 sec	25 min 10 sec
	M	49 » 30 sec	5 » 35 sec	15 » 08 »	14 » 22 sec	29 » 20 »

TABLE 2
Changes in the Arterial Blood Pressure during the First Hour of Resuscitation (average values)

Experimental series	Arterial blood pressure, mm Hg							
	original level	during the resuscitation after the reappearance of spontaneous breathing						
		immediately	after					
			5 min	10 min	20 min	30 min	40 min	60 min
Hypophysectomized animals	129	63	109	96	87	68	55	30
Control animals	157	127	138	123	106	107	106	92

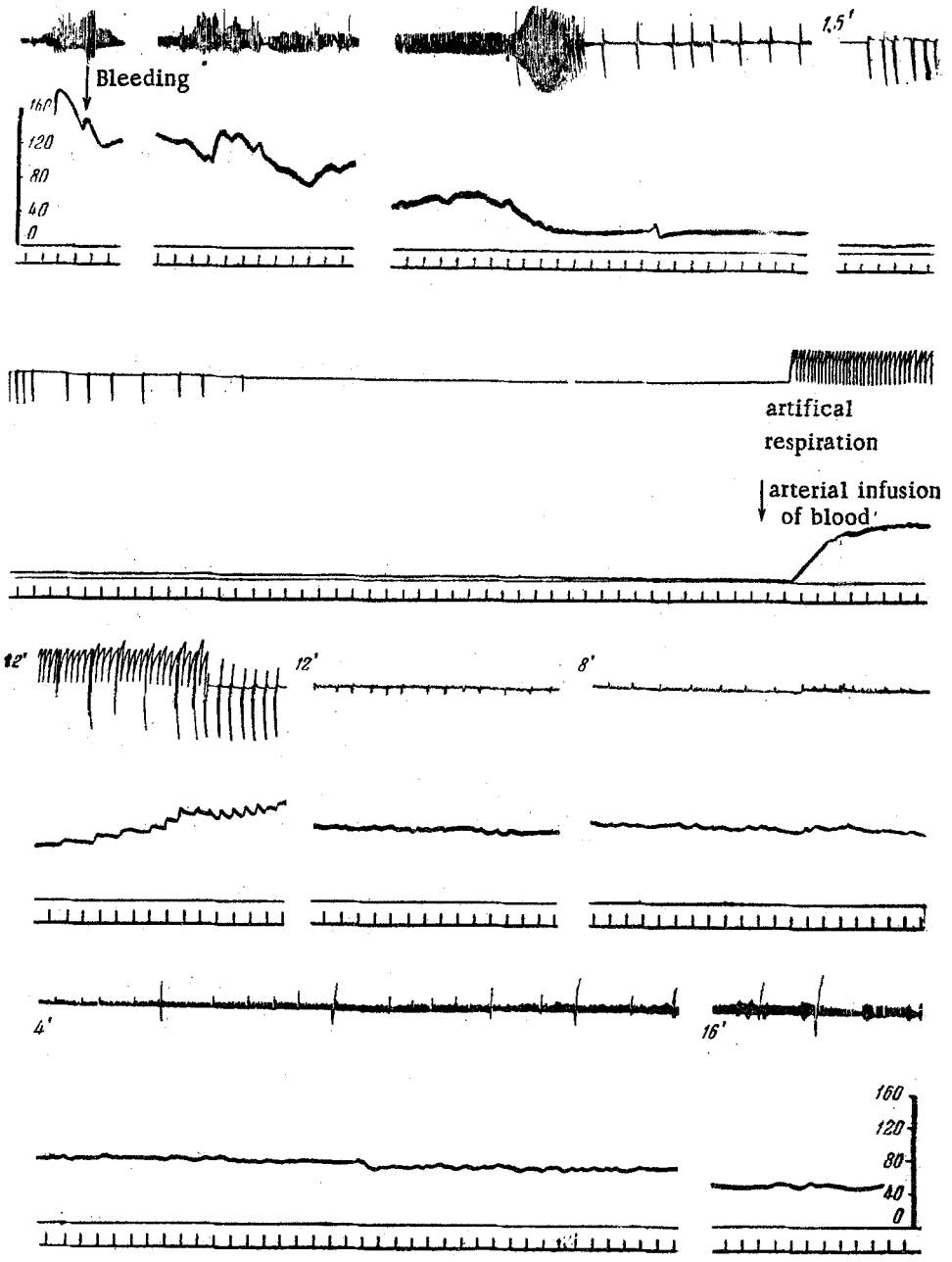

Fig. 1. Restoration of the vital functions after clinical death in a cat after removal of the anterior lobe of the pituitary gland in an experiment performed on October 8, 1959. 60 mins after reappearance of spontaneous breathing the arterial blood pressure decreased to 50 mm. Significance of curves (from top to bottom): respiration; arterial blood pressure; zero line; time mark (10 secs).

the basilar bone which is bleeding to a moderate degree. The bone was trepanated by means of a perforating machine using a multi-blade drill; this secured the precise approach to the pituitary gland and also haemostasis by the bone borings. The dura mater was dissected before the papilla (a residue of the craniopharyngeal duct mentioned above). The adenohypophysis was squeezed through the opening under the influence of the intracranial pressure and was removed to its full extent by means of a small sharp spoon. After this the posterior lobe of the pituitary gland was well visible and could be removed. The floor of the wound canal was covered by a fibrin-membrane; the defect in the bone was sealed with cement-phosphate.

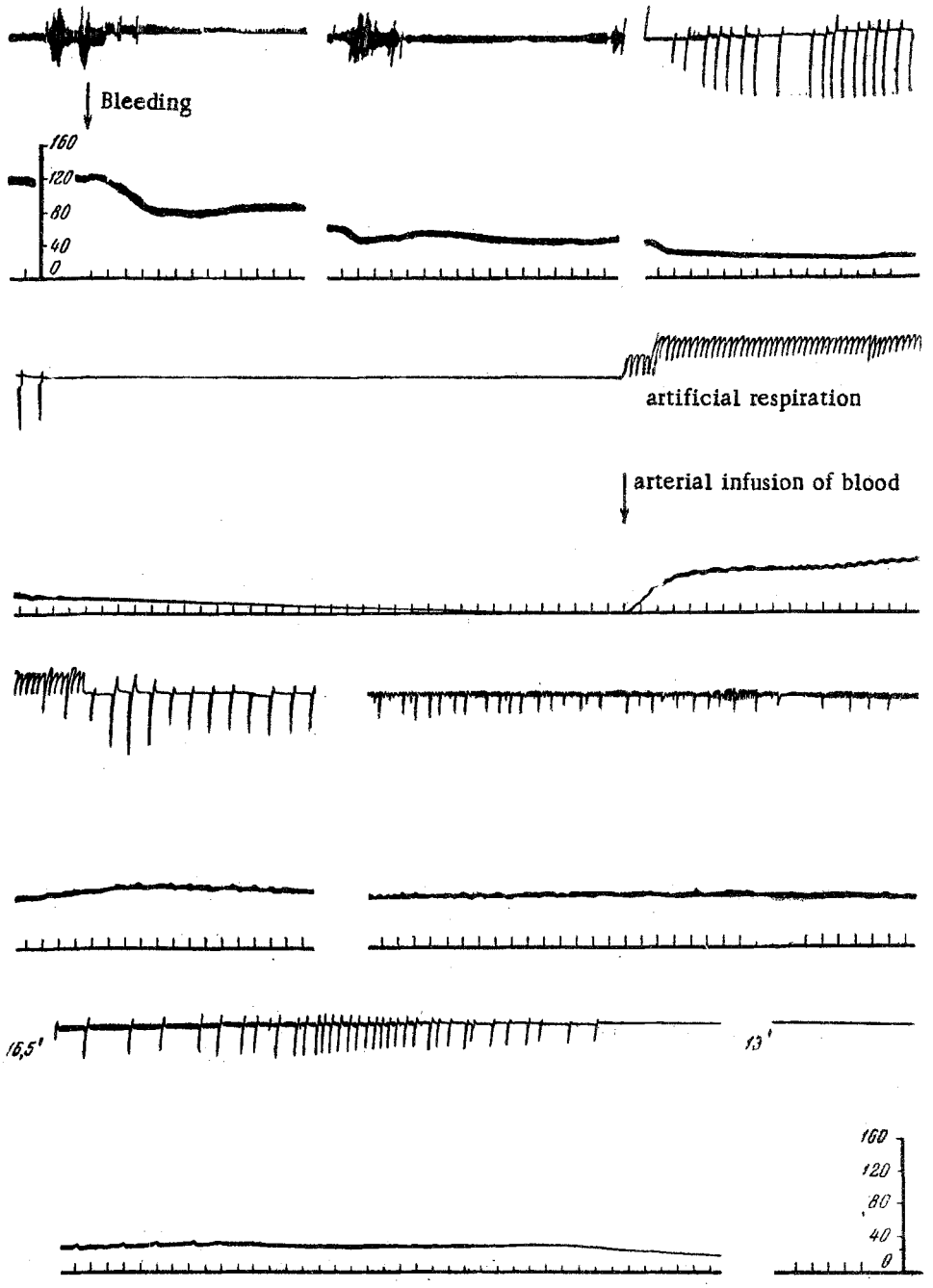

Fig. 2. Restoration of the vital functions after clinical death in a cat deprived of the arterial lobe of the pituitary gland in an experiment performed on April 27, 1960. 44 mins after reappearance of spontaneous breathing the animal perished. Significance of curves same as in Fig. 1.

In the post-operative period the animals were treated with penicillin and the saline solution recommended for adrenalectomy [19]. After two weeks the animals were used for the basic experiment. Death was caused by fractionated bleeding (in portions of blood corresponding to 0.75% of the body weight at intervals of 15-20 mins) from the common carotid artery. The revival was performed by the method of V. A. Negovskii with heparinized blood from the same animal without addition of glucose and as far as possible without addition of adrenalin as accepted in the studies of G. L. Lyuban and co-workers [11]. The blood for analysis was collected in the beginning and at the end of the bleeding period and during the revival 20, 40 and 60 min after the reappearance of spontaneous breathing.

RESULTS

A prolonged state of death caused by fractionated bleeding exhausts the compensatory possibilities of the animal body and makes resuscitation difficult [5, 10]. Under these conditions removal of the anterior lobe of the pituitary gland has an unfavorable effect upon the restoration of the vital functions but this effect does not become immediately manifest. Our experiments showed that hypophysectomized animals survived the state of clinical death and can be brought out of that state by the usual methods of resuscitation. Restoration of the cardiac function the vasomotor and the respiratory center as well as the cornea reflexes could be observed.

It is a fact deserving attention that spontaneous breathing reappears more rapidly in hypophysectomized animals (Table 1).

It was assumed that the earlier restoration of breathing in the experimental animals was connected with the lesser duration of the process of dying and the clinical death. Our findings show however that this is not always the case (experiments No. 9 and 10). The earlier appearance of spontaneous breathing during the revival of animals deprived of the anterior lobe of the pituitary gland may possibly be caused by peculiarities of their metabolism. This assumption requires special experimental investigation.

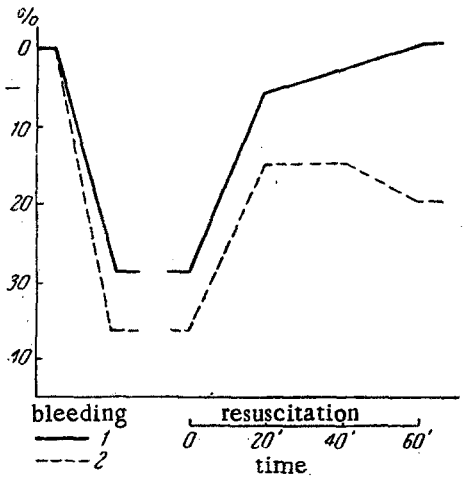

Fig. 3. Changes in the haemoconcentration in the experimental animals.. 1—control animals, 2—hypophysectomized animals.

The pattern of changes in the arterial blood pressure reflects the course of resuscitation (Table 2). At the moment spontaneous breathing reappears the arterial blood pressure is in the hypophysectomized animals only half as low as in the control animals. Later the arterial blood pressure rises but does not reach the level of the control animals.

Later on during the first hour of resuscitation the arterial blood pressure of the hypophysectomized animals continually decreases. Almost one half of the animals (four out of ten) perished between the 40th and 60th minute of the resuscitation period. The above tendency in the changes of the arterial blood pressure is illustrated by photocymograms (Fig. 1 and 2).

Resection of the anterior lobe of the pituitary gland had also an effect upon the haemoconcentration (Fig. 3). As the quantity of blood measured after the bleeding proved to be lower in the experimental animals than in the control animals it could be assumed that the greater degree of dilution found in the blood of hypophysectomized animals was not due to an increased mobilization of liquid into the blood stream but rather to a deposition of formed elements. If one compares the pattern of changes in the arterial blood pressure and in the haemoconcentration it appears that in the second half hour of the resuscitation period the arterial blood pressure decreases in the control animals and the haemoconcentration increase, returning to the original level. In the hypophysectomized animals however the haemoconcentration notwithstanding the marked fall in the arterial blood pressure not only fails to increase but even decreases further.

The experiments thus showed that the pituitary gland exerts a peculiar effect upon resuscitation. Our results coincide in the main with the findings of previous investigations carried out on adrenalectomized animals [8]. According to contemporary conceptions loss of the function of the anterior lobe of the pituitary gland leads to adrenal failure [1, 18, 20].

At an earlier stage of resuscitation when the cerebral cortex and the subcortical centers are in a state of profound inhibition the loss of the pituitary influence does not become particularly manifest. The pituitary-adrenal failure became manifest at a later stage during the restoration of the mesencephalic and diencephalic function.

It can be assumed that under normal conditions during the resuscitation of healthy animals the role of hormonal deficiency will become particularly manifest during the period of restoration of the higher prats of the central nervous system and during the normalization of the metabolism. At the time when the subcortical centers and the reticular formation are inhibited, the secretion of hormones by the adenohypophysis will cease [13, 1, 17].

Afer the function of the hypothalamus has been restored the pituitary gland begins to function again which leads to the mobilization of coricoid hormones which directly participate in the elimination of the metabolic disorders and thus enhance revival. Disruption of this physiological mechanism (removal of the pituitary gland, adrenalectomy, functional failure)may render a resuscitation difficult.

SUMMARY

The course of resuscitation was compared after fatal blood loss in hypophysectomized and healthy cats. Experiments have demonstrated that removal of the anterior lobe of the hypophysis impedes the restorative process. Hypophyseal-adrenal insufficiency becomes manifest during functional normalization of the subcortical centers and metabolism. ACTH and cortisone therapy is recommended in terminal conditions.

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