THE ROLE OF THE ADRENALS IN THE RESTORATION OF THE VITAL FUNCTIONS AFTER CLINICAL DEATH*

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Resuscitation after clinical death depends primarily on restoration of the functions of the central nervous system, which is most sensitive to oxygen lack [9, 10].

Restoration of the disturbed central control determines the subsequent vital activities of the body and the normal functioning of its effector systems and organs. At the same time it must be borne in mind that disturbances of metabolism have an effect on the centers of the brain. Even in the period of restoration of the activity of the midbrain and of the appearance of bioelectrical activity in the cortex, glycolytic processes are still predominant over oxidative, and the blood contains an increased amount of organic acids [2, 11].

Incompletely oxidized products of metabolism and toxic substances formed in the tissues during oxygen starvation may have an unfavorable effect on the restoration of the functions of the brain. In this connection it is important to study the role of the adrenal glands in resuscitation, for as effectors of the second order [3], they play a direct part in the processes of metabolism, or, according to the findings of several workers, they bring about neutralization of the toxemic factors [1, 4, 15 and others].

With this in view, we studied resuscitation after clinical death in adrenalectomized animals, some of which, for replacement therapy, received cortisone and a special salt-rich diet [8]. Resuscitation of the adrenalectomized animal was first carried out in V.A. Negovskii's laboratory in order to discover the role of the adrenals in disorders of carbohydrate metabolism [2].

EXPERIMENTAL METHOD

The experiments were carried out on cats of both sexes. A one-stage bilateral adrenalectomy was performed under intratracheal ether anesthesia, with sterile precautions, through a retroperitoneal approach. The animals of series A were used in the experiment from 16-17 hours after adrenalectomy. Experiments on 10 animals showed that the length of survival of cats after one-stage bilateral adrenalectomy varied between wide limits – from 23 to 158 hours (average – 60 hours).

The experiments in series B were carried out on animals 4 days after adrenalectomy. For 3 days after the operation the animals received cortisone (10 mg/kg once daily). The last injection of the drug was given 24 hours before the experiment. The mineral balance and nutrition were maintained by the administration of salt solution and milk through a tube. The experiments in series C were performed 4 days after adrenalectomy. In the postoperative period the animals received large doses of cortisone (10 mg/kg twice a day), salt solution and milk. The last injection of cortisone was given just before the experiment. Clinical death was induced by bleeding. From 4-5 minutes after the last breath of the animal in a state of agony, resuscitation by V. A. Negovskii's method was commenced, without addition of glucose to the blood and, so far as possible, without adrenalin.

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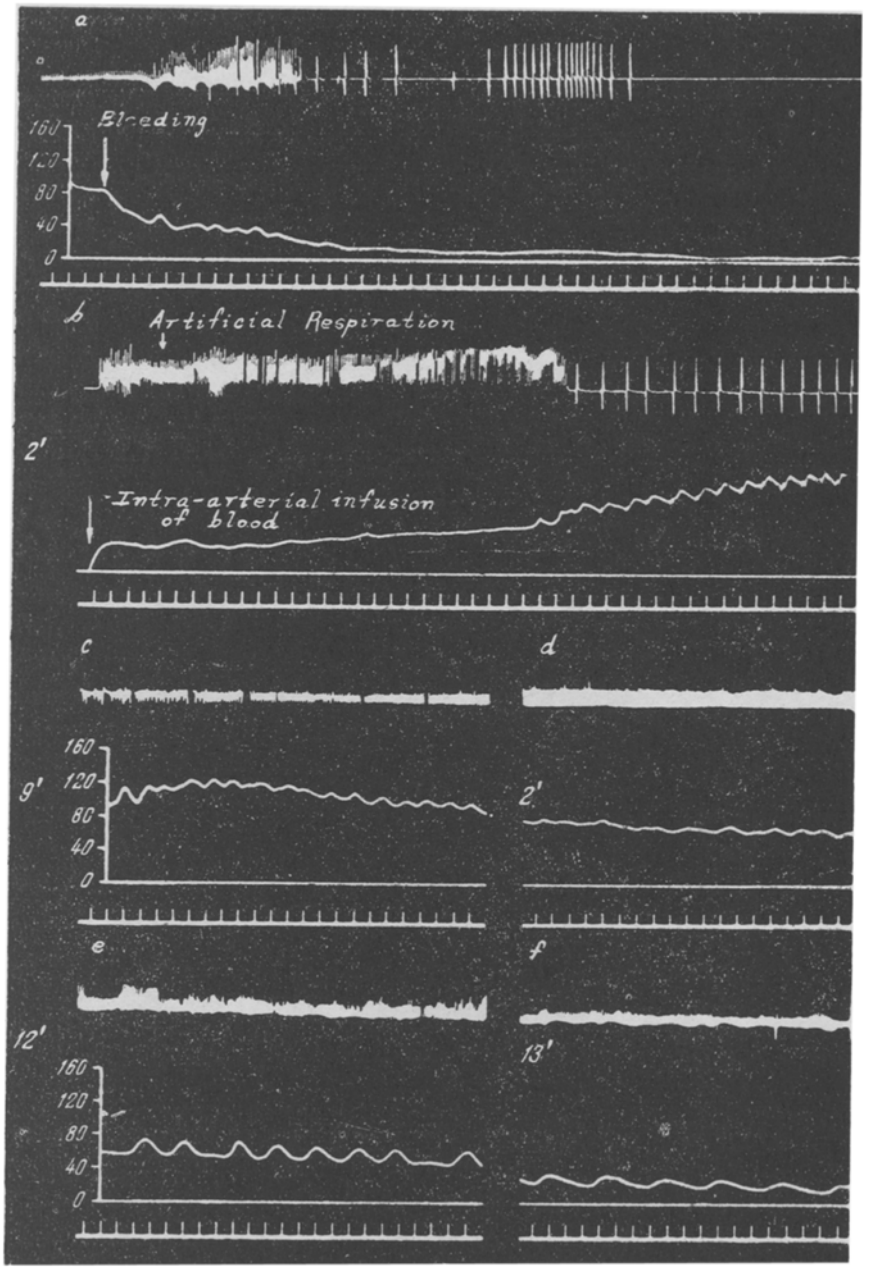

Fig. 1. Restoration of the vital functions after clinical death of a cat in an experiment dated March 30, 1958, using artificial respiration and intra-arterial infusion of blood.

a) Bleeding, onset of clinical death; b) resuscitation and period of independent agonal respiration; c) 9 minutes after restoration of spontaneous respiration; d) 11 minutes after restoration of spontaneous respiration; e)12 minutes after. Significance of the curves from above down: respiration, arterial pressure, zero line and time marker - 10 seconds.

EXPERIMENTAL RESULTS

The adrenalectomized cats (16-17 hours after adrenalectomy) could be brought out of the state of clinical death by means of artificial respiration and arterial blood transfusion in the majority of cases even without administration of adrenalin (Fig. 1).

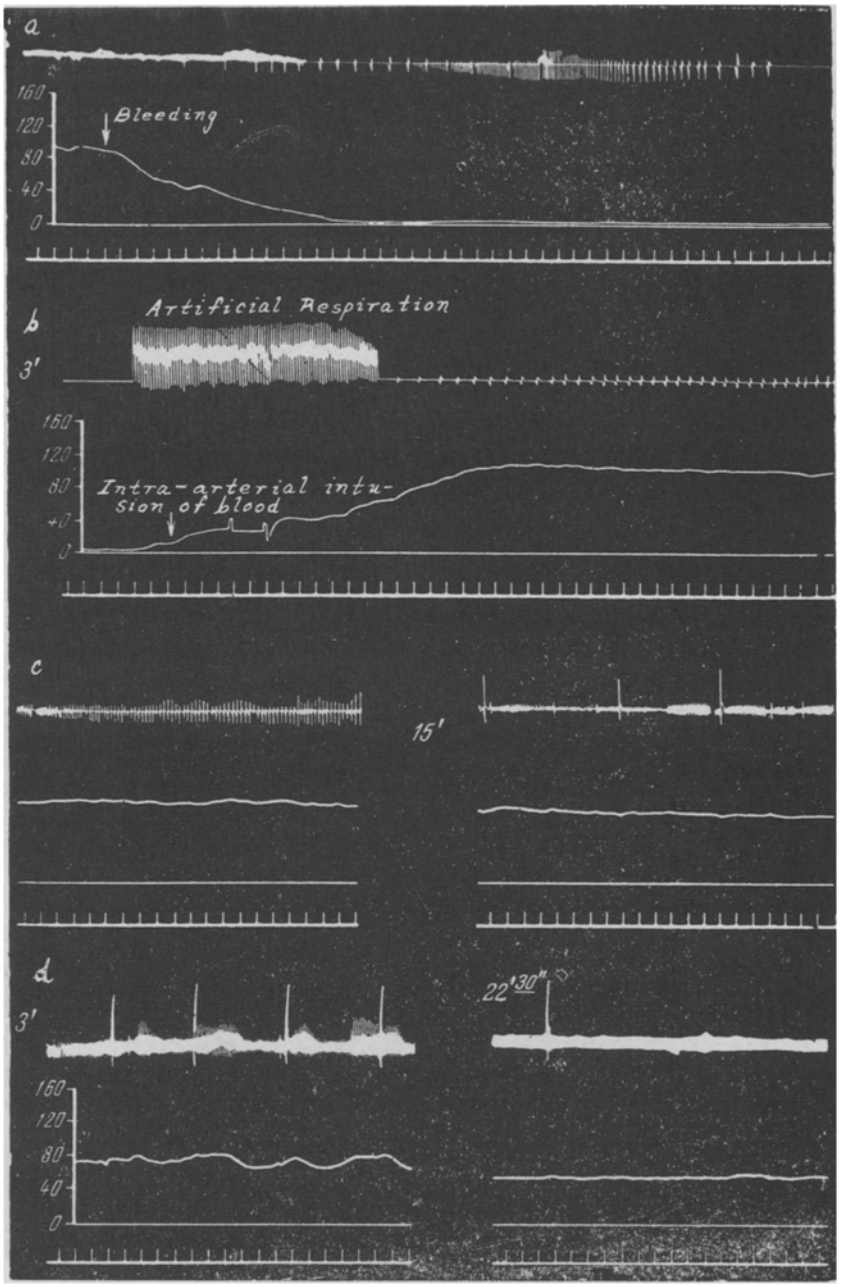

Fig. 2. Restoration of the vital functions after clinical death of a cat in an experiment dated April 11, 1958, in which cortisone was injected in the postoperative period. Legend as in Fig. 1.

During resuscitation the blood pressure and respiration were rapidly restored, but the subsequent normalization of the vital functions was much more difficult. The suggestion was made that the subsequent normalization of functions by resuscitation of animals may depend on the presence of adrenal hormones. At the same time it was impossible to exclude the effect of operation trauma, involving both injury to the nerve plexuses in the region of the operative field and failure of the function of the adrenals. For this reason in the next series of experiments the animals were taken 4 days after adrenalectomy. In the postoperative period, small doses of cortisone were injected and a high salt diet was given. The experiments showed that in these animals a relatively rapid restoration of the cardiac activity and of respiration were observed during resuscitation after clinical death (Fig. 2). However the normalization of the vital functions later on was also inadequate here.

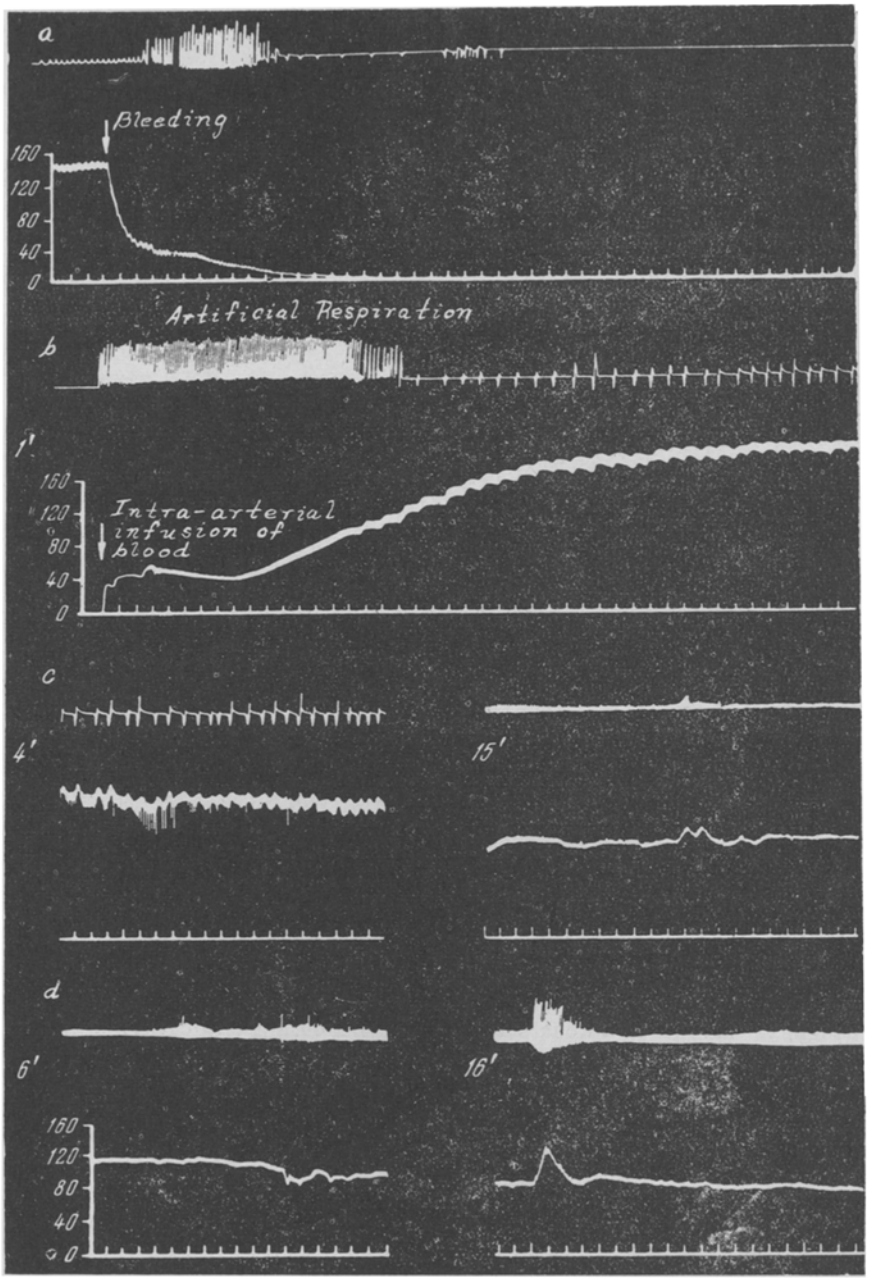

Fig. 3. Restoration of the vital functions after clinical death of a cat in an experiment dated May 24, 1958, in which large doses of cortisone were injected regularly in the postoperative period. Legend as in Fig. 1.

In the last series of experiments (c), after adrenalectomy the animals received a large quantity of cortisone throughout the entire postoperative period. During resuscitation after fatal blood-loss in these animals, the level of the blood pressure and the respiration were rapidly restored (Fig. 3). The normalization of the functions in the recovery period in this series of experiments was carried further. It is interesting to compare the results with those of resuscitation of normal healthy animals, as obtained in a joint investigation by G. L. Lyuban and one of us. In Table 1 are shown the mean values of the main indices characterizing the stage of dying and the first period of restoration of the vital functions after clinical death.

It must be pointed out that the adrenalectomized cats died after a smaller blood-loss than the healthy cats.

TABLE 1

Indices Characterizing the Stage of Dying and Resuscitation of Cats after Clinical Death

Series of experiments	Duration			Number of experiments	
	of stage of dying	of clinical death	of restoration of respiration	total	in which adrenalin was used
Healthy animals	7′42″	5′	6′30″	10	2
Series A	6′40″	4′38″	3′50″	10	3
» B	7′36″	4′48″	7′58″	10	4
» C	8′40″	4′45″	4′17′	10	3

TABLE 2

Changes in the Arterial Pressure of Cats During the First Hour after Resuscitation

Series of experiments	Arterial pressure in mm of mercury (mean values)								
	original	after resuscitation							
		at the moment of appearance of spontaneous respiration	5′	10′	15′	20′	30′	40′	60′
Healthy animals	155	100	165	140	125	120	130	137	125
Series A	98	84	124	100	96	85	85	62	40
» B	104	66	93	95	87	84	81	86	56
» C	114	68	105	128	121	104	109	106	88

TABLE 3

Length of Survival of Adrenalectomized Cats Enduring Clinical Death

Experiment No.	Length of survival of animals, series of experiments		
	A	B	C
1	1 hr 07 min	1 hr 05 min	14 hr
2	0 hr 57 min	2 hr 30 min	10 hr
3	1 hr 07 min	4 hr	7 hr
4	2 hr 40 min	3 hr 40 min	15 hr
5	1 hr 50 min	1 hr 10 min	13 hr
6	1 hr 50 min	1 hr 05 min	10 hr
7	2 hr 07 min	2 hr 40 min	14 hr
8	1 hr 28 min	2 hr	3 hr
9	1 hr 10 min	8 hr	5 hr 45 min
10	1 hr 25 min	1 hr 50 min	3 hr
Average	1 hr 35 min	2 hr 50 min	9 hr 30 min

In view of the equal duration of the stage of dying and of clinical death in the adrenalectomized animals, the difference which was found in the restoration of respiration must evidently be attributed to variations in the management of the postoperative period. This stage of affairs calls for further experimental investigation.

As may be seen from Table 2, the blood pressure in the adrenalectomized animals at the beginning of the experiment was lower than in the healthy cats, but was close to the physiological normal level.

In the period of restoration of the vital functions after clinical death in the series A experiments (16-17 hours after adrenalectomy) and the series B experiments (4 days after, with small doses of cortisone) the arterial pressure fell considerably, and reached at the 60th minute a level which threatened the vital activity of the animal.

Attention was drawn to the slight increase in the blood pressure of healthy animals 30-40 minutes after the appearance of spontaneous respiration. At this time the ocular reflexes had been restored in the animals, the respiration quickened, the muscle tone increased, and a motor reaction was periodically observed, which showed the restoration of the functions of the midbrain [9, 10].

In adrenalectomized animals at the 30th-40th minute of resuscitation, an increase of blood pressure, although very slight, was observed in the experiments in which large doses of cortisone were given (series C).

Later on all the adrenalectomized animals which had endured clinical death died at various times after the moment of reestablishment of spontaneous respiration (Table 3).

As the experiments showed, the adrenalectomized cats could be brought out of a state of clinical death by means of V. A. Negovskii's method. In the first period of resuscitation, judging by the restoration of the arterial pressure and the respiration, there were no special signs of adrenal deficiency. This possibly was due to the profound inhibition of the central nervous system. Characteristically the animal showed at this period considerably increased resistance to various pathological agents [5, 6, 7, 12 and others]. Subsequently, as the functions of the midbrain and diencephalon were restored, signs of deficinecy of adrenal hormones began to appear

In the experiments in which the adrenalectomized animals were "saturated" with cortisone, normalization of the functions during resuscitation was more successful. A relationship was thus revealed between the restoration of the vital functions after clinical death and the presence of the adrenal cortical hormone in the body.

In this connection it is relevant to mention the views of A. A. Bogomolets in support of the role of the adrenals in the pathogenesis of traumatic shock [1]: "It is highly probably that depression of the internal secretory activity of the adrenal cortex arises secondarily in the animal, as the result of severe disturbances of the function of the nervous system, but the inevitability of repercussion on the nervous system of the disturbances of the internal secretory activity of the adrenal cortex is perfectly obvious."

The use of cortisone in a severe terminal state,such as the period of restoration of the vital functions after clinical death when increased demands are made on the neurohumoral regulation and the absolute or relative adrenal deficiency may have an unfavorable influence on the body, appears to us to be promising. As we know, hormone therapy has justified itself in clinical practice, especially in the prophylaxis and treatment of postoperative shock [13, 14].

SUMMARY

The restoration of vital functions (Professor V. A. Negovskii's method) was studied following lethal desanguination in adrenalectomized cats.

Several groups of animals were experimented upon: observation of the first group of animals was conducted 16-17 hours after adrenalectomy, adrenalectomy with administration of saline solution and cortisone (30 mg/kg of body weight per course), on the third – 4 days after adrenalectomy with administration of saline solution and large doses of cortisone (70 mg/kg of body weight per course).

The restoration of vital functions was best in adrenalectomized animals which received large doses of cortisone. The authors believe that cortisone is of value in the therapy of terminal conditions.

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