INVESTIGATION OF CATECHOLAMINES IN VARIOUS ORGANS OF DOGS DURING DEEP HYPOTHERMIA

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In connection with the introduction of open heart operations into surgical practice, employing deep hypothermia, the study of hormones regulating the metabolic processes, and in particular the catecholamines, has acquired not only theoretical interest, but also great practical significance.

TABLE 1. Mean Concentration of Catecholamines in the Tissues of Different Organs (in Milligrams per Gram of Dry Tissue) and in the Blood (in Micrograms %) of Dogs in the Control Group, at 37°

Subject of investigation	Total concentration of cate-cholamines	dehydro forms	CSP
Adrenals	0,055	0,01	2,6
Heart	0,004	0,0004	0,5
Brain	0,0002	0,0003	1,5
Skeletal muscle	Not detected	—	—
Blood	17,0	6,0	1,2

A number of authors have studied the catecholamines experimentally, under conditions of deep hypothermia, and obtained contradictory data [9,11,13].

We performed experiments on dogs that were subjected to chilling down to 10° in the mediastinum, with subsequent warming to normal body temperature (37°).

EXPERIMENTAL METHOD

In the experiment, we used dogs weighing 17-22 kg.

The control group consisted of animals in which, following administration of narcotic, the catecholamines were investigated, at normal body temperature (37°), in the blood and in the tissues of the adrenals, the cerebral cortex, and cardiac and skeletal muscle. The concentration of catecholamines in the blood of these animals was also determined immediately before narcosis.

Anesthetization was the same in all experiments. Premedication was accomplished one hour before initiation of the experiment (morphine, 5 mg/kg subcutaneously, and promedol, 5 mg/kg); introductory anesthesia was carried out with a 1% solution of hexenal. Narcosis was induced with nitrous oxide and oxygen in the ratio of 3 : 2, and a small amount of 3-4% ether; in this case, we used a semi-open system type of apparatus, with automatically controlled respiration. Relaxants (listenone) were injected 1-2 times, in a dose of 1 mg/kg.

Chilling to a temperature of 10° in the mediastinum, and warming to 37°, were accomplished in the course of 10-15 min by the extracorporal method, using an artificial circulation apparatus.

Before attaining maximum chilling (10° in the mediastinum), the blood circulation was stopped for 15 min, and then chilled blood was reperfused and blood circulation was once again completely stopped. In the experiments, the total duration of its stoppage was 30 min. After this, the animal was warmed to normal body temperature.

The catecholamines (adrenalin-like substances and their dehydro forms) in the blood and skeletal muscle of the dogs was investigated at 5 stages: during maximum cooling, 15 min after blood circulation was stopped, before and after reperfusion, and also 30 min after blood circulation had been stopped. After warming the animal to 37°, the indicated indices were determined, plus their level in the tissues of the adrenals, cardiac muscle, and cerebral cortex.

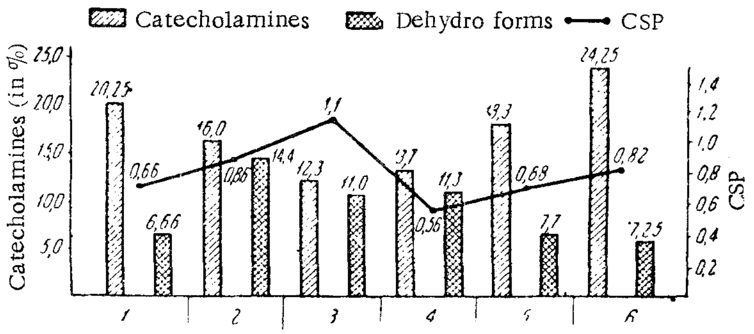

Fig. 1. Change in the concentration of catecholamines within the blood of dogs during deep hypothermia (mean data). 1) Before chilling; 2) maximum cooling; 3) 15 min after stopping the heart; 4) after reperfusion; 5) before warming; 6) after warming.

In determining the concentration of catecholamines in the blood and tissues, we used the adsorption-colorimetric method, proposed by Whitehorn[18] and Shaw [15], with certain modifications introduced by A. M. Utevskii [7] and N. A. Smazhnova [4].

The level of catcholamines was measured after alkaline and acid treatment of the adsorbent. Acidification made it possible to demonstrate the total concentration of catecholamines (adrenalin, noradrenalin, and other, unidentified adrenalin-like substances), while, in the absence of ascorbic acid, we also measured the concentration of their dehydro forms.

In order to show the quantitative relationship for adrenalin, we calculated the coefficient of specificity (CSP), introduced in 1938 by Shaw and representing the ratio of the figures obtained after alkaline and acid treatment of the adsorbent. On the basis of the investigations of a number of authors [2,6,10,15], it is accepted fact that when the CSP is equal to or greater than 2, there is a quantitative predominance of adrenalin and an absence of noradrenalin. In those cases where the CSP is between 1 and 2, it may be assumed that both adrenalin and noradrenalin are present in the sample being tested. If the CSP is equal to, or less than 1, then basically one may speak of the presence of noradrenalin and the absence of adrenalin.

EXPERIMENTAL RESULTS

At normal body temperature, a varying total concentration of catecholamines was observed in the blood and tissues of the dogs.

Table 1 shows that the highest level of catecholamines was found in the tissues of the adrenals, where there was basically a predominance of adrenalin [3,15,16]. In the tissues of the brain and heart, their concentration was considerably lower; in this case, a predominance of noradrenalin was seen in the cardiac muscle [1,3,12], while in

TABLE 2. Total Concentration of Catecholamines (in μg-%) in the Blood of Dogs during Deep Hypothermia

Stage of the experiment	Catecholamines		Dehydro forms		CSP	
	range	mean data	range	mean data	range	mean data
Before narcosis	13,0—20,5	17,0	30—00	6,0	1,0—1,0	1,2
After narcosis.	17,0—26,0	20,25	4,0—12,0	6,66	0,4—0,82	0,66
Maximum cooling	11,0—21,0	16,0	9,0—21,0	14,33	0,54—0,99	0,86
15 min after blood circulation stopped . .	6,0—20,0	12,25	6,0—20,0	11,0	0,6—2,0	1,1
After reperfusion	12,0—15,0	15,66	6,0—15,0	11,33	0,5—0,72	0,56
Before warming	15,0—21,0	18,33	3,0—15,0	7,66	0,4—0,86	0,68
After warming	21,0—26,0	24,25	2,0—14,0	7,25	0,73—0,95	0,82

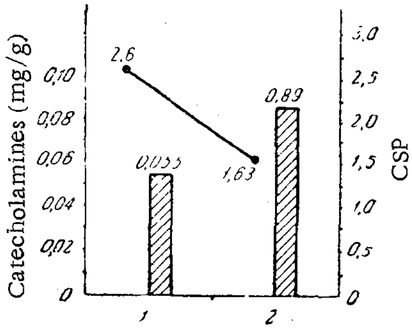

Fig. 2.

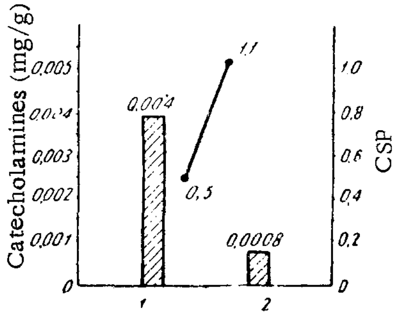

Fig. 3.

Fig. 2. Change in the concentration of catecholamines in the adrenals of dogs associated with deep hypothermia (mean data). 1) Before chilling; 2) with warming after the deep hypothermia. The remaining designations are the same as in Fig. 1.

Fig. 3. Change in the concentration of catecholamines in the cardiac muscle of dogs associated with deep hypothermia (mean data). Designations the same as in Fig. 2.

the brain tissue there was both adrenalin and noradrenalin. The extremely low concentration of catecholamines in the brain tissue may be related, in some degree, to the fact that it was determined in the cortical areas of the brain, where, according to the data in the literature [6,10,17], catecholamines are contained in extremely small amounts. We were unable to determine a catecholamine concentration in the skeletal muscle, either under normal temperature or under hypothermic conditions. Apparently, the method we used is not sufficiently sensitive to demonstrate such minimal amounts of catecholamines as are present in skeletal muscle [3].

As already indicated, the level of catecholamines in the blood under conditions of deep hypothermia was determined at all stages of the experiments.

Table 2 and Fig. 1 show that the injection of narcotic agents and anesthetics and the influence of the operation trauma all lead to an increase in the total concentration of catecholamines in the blood. The level of these substances after application of narcosis reached 20.25 μg% (versus a normal level of 17 μg%). The decrease in the CSP, observed in this case, down to 0.66, indicates that the increase in the total amount of catecholamines is basically a result of an increase in noradrenalin, with a simultaneous decrease in adrenalin.

With maximum cooling, we observed a decrease in the catecholamines within the blood. A still greater reduction in their level was noted after stopping the blood circulation for 15 minutes. This decrease was evidently at the expense of noradrenalin, as indicated by the increase in the CSP to 1.1. It is interesting to note that, simultaneously with the reduction in the amount of catecholamines within the blood, the concentration of their dehydro forms, at maximum cooling, increased by almost two times, which is apparently caused by a defense reaction of the organism, preserving the reserve forms of the hormones necessary for normal metabolic processes.

After reperfusion with the chilled blood, we observed a certain increase in the catecholamines. Subsequent heating of the organism to 37° caused an even greater rise in the catecholamines within the blood, the level exceeding the original by 40%.

TABLE 3. Mean Concentration of Catecholamines (in mg/g) in the Tissues of Different Organs of Dogs Associated with Warming the Animals to 37° after Deep Hypothermia

Subject of the investigation	Catechol-amines	Dehydro forms	CSP
Adrenals	0,083	0,03	1,65
Cardiac muscle	0,0008	0,0003	1,1
Brain	0,0003	0,0001	1,23

Concerning the dehydro forms of the adrenalin-like substances, after stopping the blood circulation for 15 min we already noted a certain decrease in their level, which then continued on into the subsequent stages.

Thus, we demonstrated a definite correlation between the rise in catecholamines and the decrease in their dehydro forms within the blood in the final stages of the operation. In explaining this fact, we join in the opinion of the authors who believe that the increase in catecholamines with simultaneous decrease in their dehydro forms characterizes a marked stimulation in the sympatho-adrenal system [4,10,14].

As already indicated, the level of catecholamines in the tissues of the adrenals, cardiac muscle, and cerebral cortex was investigated only at the final stage – after warming.

Analysis of the obtained data (Table 3) showed that warming the organism to 37°, performed after deep chilling and 30-min stoppage of the blood circulation, causes an increase in the total concentration of catecholamines within the tissues of the adrenals by more than 1.5 times, as compared with the level of these substances in the unchilled animals (Fig. 2). The associated decrease in the CSP figure to an average of 1.6, i.e., by more than 43%, as compared with the norm, indicates that the total amount of catecholamines under these conditions is elevated chiefly by an increase in noradrenalin.

A different pattern was noted in relation to the changes in these substances within the cardiac muscle (Fig. 3). We observed a marked decrease in the level of catecholamines in the cardiac muscle following warming – down to 0.0008 mg, over 2.5 times less than the original level, while against the setting of a decrease in noradrenalin, it was possible to observe a certain accumulation of adrenalin.

We were unable to establish significant changes in the catecholamine concentration within the brain tissue following the warming. The total concentration of dehydro forms of the adrenalin-like substances in the tissues of these organs also failed to undergo essential changes.

Thus, investigation of the catecholamines in the blood and tissues of dogs, under conditions of deep hypothermia, showed that there is a definite pattern to the changes in their concentration.

The level of catecholamines in the blood markedly decreases with maximum cooling of the organism, and especially after a 15-min stoppage of blood circulation. Following reperfusion with chilled blood, carried out after the 15-min circulatory arrest, we observe a negligible increase in the blood catecholamines. Subsequent warming to normal body temperature causes an increase in the level of catecholamines, exceeding the original figure by 40%. It should be pointed out that this fact is apparently connected with an increase in the intensity of catecholamine secretion within the adrenals. This is evidenced by the increase which we encountered in their concentration within the gland, following warming, by more than 1.5 times, as compared with this concentration in the unchilled animals.

Thus, the observed changes in catecholamine concentrations are reversible in nature, as indicated by the elevation in their level after the animals are warmed.

Assuming that the catecholamines (especially adrenalin) exert a stimulatory effect on oxidative processes, it is probable that the demonstrated decrease in their concentration within the blood following deep hypothermia to some degree causes a reduction in the tissue oxygen requirement. In connection with this, we would like to point out the work of E. P. Stepanyan, E. P. Geselevich, et al. [5], who made parallel studies of tissue respiration and adenosinetriphosphatase activity in these animals, and observed a significant decrease in these indices within all the tissues that were investigated.

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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.