

THE ROLE OF ASCORBIC ACID IN THE MECHANISM OF ARTIFICIAL HYPOTHERMIA DEVELOPMENT

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 52, No. 7, pp. 54-57, July, 1961

Original article submitted July 26, 1960

Ascorbic acid plays an important part in the vital activity of the organism, and disturbance of its metabolism has serious consequences. Ascorbic acid actively participates in the formation of the adrenal cortical and medullary hormones [6,8,9,14,18,21], which are produced intensely when the organism is acted upon by extraordinarily strong stimuli. The brief application of a cold stimulus causes a marked decrease in the ascorbic acid content of the adrenal glands [2,10,12,13,16,17,20]. When the cold influence is prolonged, if the animals adapt to the low temperature conditions, the amount of ascorbic acid in the adrenal glands increases considerably [12,15]. When the animal organism is saturated with ascorbic acid, the usual hypertrophy of the adrenal glands in response to a cold stimulus is not observed [12], and the animals become more resistant to cold. The development of hibernation depends to a large extent on the ascorbic acid content of the blood and tissues; animals not sufficiently saturated with ascorbic acid (gophers) do not fall asleep [1].

All these data indicate the essential role of ascorbic acid in the metabolic processes with the action of cold stimuli. This work deals with the role of ascorbic acid in the mechanism of artificial hypothermia development.

METHOD

We used the following method [19] to quantitatively determine ascorbic acid: a trichloroacetic extract of the blood or adrenal tissue was shaken with activated charcoal to oxidize the ascorbic acid into dehydroascorbic acid. If thiourea was present, phenyllosazone formed when the charcoal filtrate was incubated with 2,4-dinitrophenylhydrazine. The addition of an 85% sulfuric acid solution caused a yellowish-red color to appear, the intensity of which was colorimetrically measured on a FEK-M photoelectrocolorimeter. The ascorbic acid content of the blood and adrenal glands was calculated by comparison with a colorimetric curve constructed from a standard solution of ascorbic acid.

We examined 77 rabbits of both sexes, 13 of which served as the control. Artificial hypothermia was induced by the method employed in the clinic directed by V. I. Kazanskii [3,4,7]. The material was processed by the minor choice method of variational statistic investigation, determining the average indices, their average errors and the significance of the changes \bar{t} . The changes were considered to be significant if $t \geq 3$.

RESULTS

Our analysis of the material showed that during the fall of body temperature, when the blood and adrenal glands of the animals were taken for examination, specific patterns of change could be established within certain temperature ranges. We divided the whole experimental temperature interval accordingly into three unequal parts: 31-26, 26-25 and 25-23 deg. We then proceeded to evaluate the changes which occurred in the ascorbic acid content of the adrenal glands and blood and in the weight of the adrenal glands during each of these temperature ranges.

The experimental results are shown as average indices in the table.

Under conditions of moderate hypothermia, i. e., within the 31-26 deg temperature range, we observed a

rather pronounced and statistically wholly significant decrease in the ascorbic acid content of the adrenal glands and a concurrent increase of its content in the blood, attended by a slight, statistically insignificant increase in the weight of the adrenal glands.

Change in the Ascorbic Acid Content of the Adrenal Glands and Blood and in the Weight of the Adrenal Glands in Rabbits During the Development of Artificial Hypothermia (in Average Indices)

Number of experiments	Range of rectal temperature	Ascorbic acid in adrenal glands (in mg%)	Ascorbic acid in blood (in mg%)		Weight of adrenal glands (in mg)
			Norm	Hypothermia	
13	37—38° (control)	260.0±38.0	—	—	110.07±8.43
41	31—26°	133.3±9.2 (<i>t</i> =3.24)	0.80±0.07	1.65±0.07 (<i>t</i> =8.5)	134.43±13.3 (<i>t</i> =1.55)
13	26—25°	85.07±14.3 (<i>t</i> =4.31)	0.66±0.1	1.85±0.1 (<i>t</i> =8.5)	68.6±11.5 (<i>t</i> =2.90)
10	25—23°	246.0±19.9 (<i>t</i> =0.33)	1.08±0.1	1.32±0.13 (<i>t</i> =1.5)	112.8±7.8 (<i>t</i> =0.24)

When hypothermia increased to the 26-25 deg range of temperatures, a further and more definite decrease in the ascorbic acid content of the adrenal glands was observed, attended by a sharp increase in its content in the blood. These changes from the original levels were found to be fully significant. In this temperature range, however, no increase in the weight of the adrenal glands attended their loss of ascorbic acid; on the contrary, their average weight was much less than it had been in the temperature range of 31-26 deg and substantially lower than the average weight of the adrenal glands in the control experiments.

In the temperature range of 25-23 deg, under conditions of deep hypothermia, the rather substantial changes observed in the experimental indices were the reverse of those previously noted: the average ascorbic acid content of the adrenal glands increased considerably, while the saturation of the blood with ascorbic acid decreased sharply, approximating the average indices determined at normal body temperature. The average weight of the adrenal glands increased until it approximated that of the control animals.

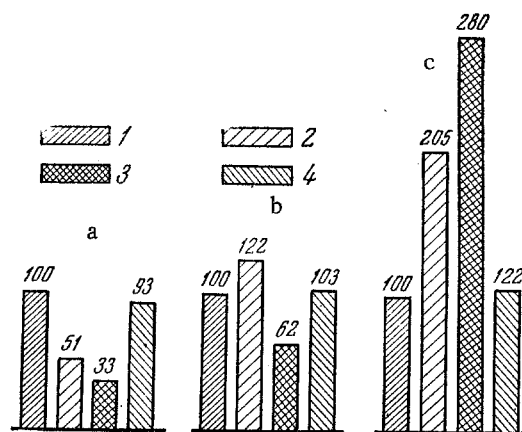
The figure shows the changes in the ascorbic acid content of the adrenal glands and blood and in the weight of the adrenal glands in the experimental temperature ranges, expressed in percent of the original levels or the control experiments.

Under our experimental conditions, premedication with a lytic cocktail considerably inhibited, but did not completely depress the organism's reaction to the cold stimulus.

In the 31-26 deg range of temperatures, there was a moderate increase in the weight of the adrenal glands. The adrenal function exhibited the adaptation syndrome, and the ascorbic acid in the adrenal glands was utilized in the production of steroid hormones. The increase in the ascorbic acid content of the blood could indicate that the amount of this substance required by the organs and tissues had decreased considerably due to the reduced intensity of the metabolism and the diminished expenditure of energy [5].

When hypothermia passed into a temperature range of 26-25 deg, premedication with a lytic cocktail could no longer maintain the hypophyseal-adrenal system in a state of moderate stress. The ascorbic acid content of the adrenal glands decreased sharply; ascorbic acid was not, however, utilized by the adrenal glands to synthesize steroid hormones due to the considerable disturbance of the adrenal function. This is indicated by the acute decrease in the weight of the adrenal glands. Excessive amounts of ascorbic acid passed from the adrenal glands into the blood.

The further development of hypothermia to a 25-23 deg range of temperatures, according to the literature



Dynamics of change in ascorbic acid content under conditions of hypothermia: a) ascorbic acid content of adrenal glands (in mg%); b) average weight of adrenal glands (in mg); c) ascorbic acid content of blood (in mg%); 1) norm; 2) 31-26 deg; 3) 26-25 deg; 4) 25-23 deg.

data [11, 22], results in depression of the function of the higher, regulatory sections of the hypophysial-adrenal system, and this, evidently, to a large extent adapts the adrenal function to conditions of deep hypothermia. This is shown by the increased ability of adrenal gland tissue to concentrate ascorbic acid and by the partial restoration of their synthetic ability, which leads to an increase in their weight. It is possible that the ascorbic acid in the blood decomposes under these conditions, changing into the oxidized, dehydroascorbic form [2].

At this stage of hypothermia, the apparent equilibrium of the adrenal function is by no means stable, but rather indicates areactivity of the organism and the acute depression of all the vital functions; this leads to disturbance of the activity of the respiratory and cardiovascular systems, which is a well-known and frequent cause of death in patients or experimental animals operated upon under deep hypothermia.

All these data further confirm the essential role of ascorbic acid in the development mechanism of hypothermic conditions.

SUMMARY

The change of ascorbic acid content was studied in adrenal glands and blood of rabbits during the development of artificial hypothermia; changes occurring in the weight of adrenal glands were recorded as well. A reduction of ascorbic acid content in the adrenal glands takes place in conditions of moderate hypothermia at temperatures ranging from 31 to 26°C; there was also a moderate increase in the weight of the glands and a rise of ascorbic acid content in the blood. With intensification of hypothermia at temperatures ranging from 26 to 25°C a marked drop of ascorbic acid content in adrenal glands is accompanied by a reduction of their weight and discharge of ascorbic acid into the blood. In deep hypothermia (25-23°C) the amount of ascorbic acid in adrenal glands rises, their weight increases, while the blood ascorbic acid content declines.

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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.
