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STUDIES IN HYPOTHERMIA

- USSR -

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- USSR -

[Following is a translation of two articles in the Russian-language book Iskusstevennaya Gipotermiya (Artificial Hypothermy), Tashkent, 1961. Bibliographic information accompanies each article.]

TABLE OF CONTENTS

I. THE EFFECT OF HYPOTHERMY ON THE DEVELOPMENT OF HEMOTRANSFUSION AND ANAPHYLACTIC SHOCK

/Following is a translation of an article in the Russian-language book Iskusstvennaya Gipotermiya (Artificial Hypothermy), Tashkent, State Medical Publishing House, Ministry of Health Uzbek SSR, 1961, pages 3-7./

N. Kh. Abdullayev, Chair of Pathological Physiology, Tashkent State Medical Institute

Data which attest to the possibility of decreasing reactivity under conditions of hypothermy (A. Laborit, N. N. Sirotinin, I. P. Petrov, V. S. Galkin, V. A. Saakov, etc.) prompted us to investigate the effect of hypothermy on the course of hemotransfusion and anaphylactic shock.

The experiments were performed on 85 dogs. Hemotransfusion shock was produced by the intravenous introduction of 5 ml of preserved human blood per one kg of animal weight. In the experiments with anaphylactic shock, the dogs were sensitised by the Bidle-Kras method. Hypothermy was achieved by the use of neuroplegic, antihistamine agents and by physical cooling. The body temperature of the animals was lowered to 27-28° C.

A typical picture of hemotransfusion shock was observed in control experiments after the introduction of heterogeneous blood. The change in arterial pressure often had a four-phase nature. Blood pressure dropped to 50-60 mm, whereas the initial pressure was 120-160 mm. Shock hypotension lasted about 25-35 minutes, after which the blood pressure rose rapidly and approached its initial value.

Changes in the morphology of the blood and the blood sugar concentration were typical for the shock symptom complex.

In animals subjected to hypothermy, the maximum blood pressure was usually established within the limits of 80 and 90 mm. A typical picture of hemotransfusion shock developed in all experimental animals after transfusion of preserved human blood. Changes in blood pressure were often of a two-, three-, or four-phase nature. The initial pressor phase was usually weakly expressed, and was absent on the whole in some of the animals. The shock phase of the change in hemodynamics was more pronounced and prolonged. (Figure 1).

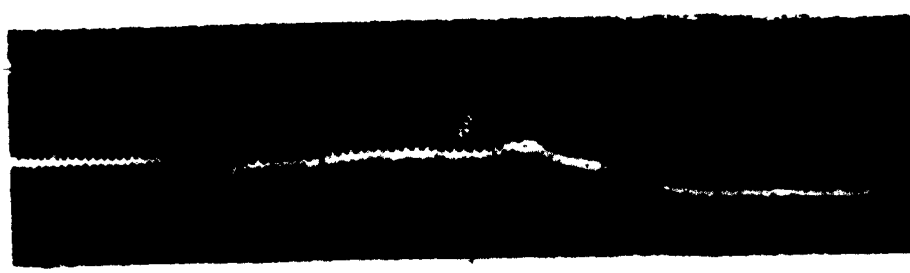

Figure 1. Heterotransfusion against a background of hypothermy. 1 - respiration; 2 - blood pressure; 3 - time reference markers; 4 - signal.

Maxim m arterial pressure fell to 20-30 mm, remaining at this level for an average of 45-50 minutes. The increase in

blood pressure after this period occurred slowly and, within 1-1.5 hours after heterotransfusion, it was restored to its level at a body temperature of 27-28° C.

Unlike the case of control animals, heterotransfusion did not cause any particular changes in respiration in dogs subjected to hypothermy.

Changes in the morphology of the blood and the blood sugar contentration were more pronounced than in the control animals.

As a number of investigators have indicated (I. P. Petrov, B. S. Saakov, M. L. Garfunkel', etc.), the blood pressure is lowered by the use of neuroplegic, antihistamine agents and physical cooling. This was also the case in our experiments. A low level of blood pressure can be reflected by the outcome of heterotransfusion under conditions of hypothermy. However, the research performed showed that if low blood pressure in animals under hypothermy is increased by the introduction of type-specific Belen'kiy serum (10 ml per one kg of animal weight), heterotransfusion also leads to the development of shock hypotension.

It is seen from these data that hypothermy not only does not prevent, but even contributes, to the development of shock, aggravating hemodynamic disturbances.

As results of the investigations showed, reflexes from the baroreceptors, which were generated by pressing on the common carotid arteries for 10 and 25 seconds, were depressed after the introduction of aminazine, lidol, and dimedrol, and usually did not appear in the state of hypothermy.

The intravenous introduction of acetylcholine (one ml in a 1:20,000 dilution), which leads, in the initial condition, to a 60-75 mm drop in blood pressure in the course of 25-40 seconds, causes a less pronounced depressor reaction (25-35 mm) against a background of hypothermy, but with more prolonged action--up to 2 minutes (Figure 2).

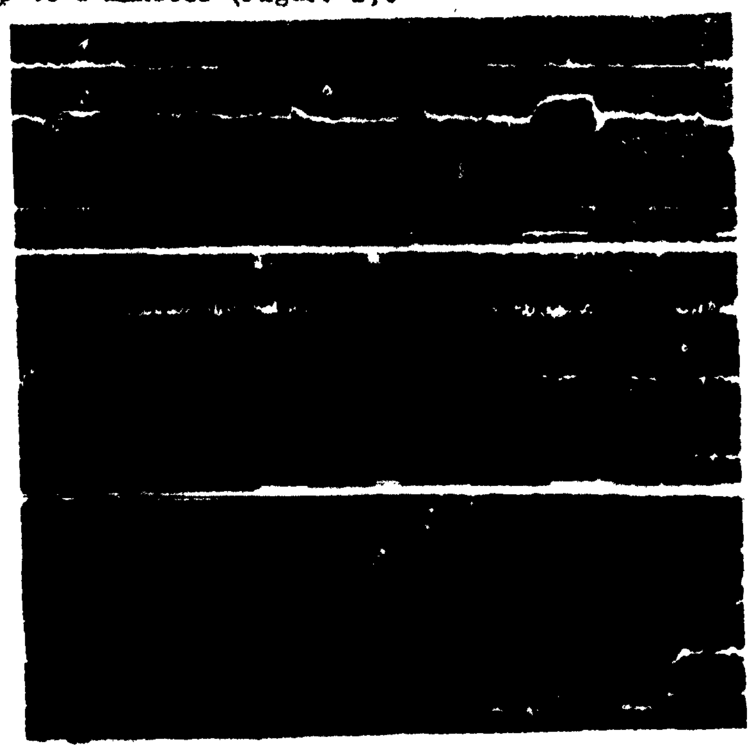

Figure 2. Testing of reflexes from baro- and chemoreceptors to the introduction of acetylcholine (designations are the same as for Figure 1).

The intravenous introduction of adrenalin (one ml 1:10,000 and 1:1,000) and ephedrine (one ml 1:500) in the initial condition lowered blood pressure by 100-70 mm. A hypotensive effect occurred, as a rule, after the introduction of these substances in a state of hypothermy, wherein the introduction of adrenalin was accompanied not only by a 30-40 mm drop in blood pressure, but also by phenomena of disturbance in the rhythm of heart activity.

These data prompted us to perform an investigation with the combined use of hypothermy and novocain for additional action on the chemoreceptors and diminution of reflex excitability.

Heterotransfusion given to animals in a state of hypothermy 15-20 minutes after the introduction of novocain (20 mg per one kg of animal weight, 1% solution) also caused the development of a typical shock sumptom complex with a 50-60% drop in blood pressure in comparison with the initial pressure.

Investigation of the effect of hypothermy on the course of anaphylactic shock showed that reinjection of antigen under conditions of hypothermy causes a different reaction. In some animals, a resolving dose of antigen does not cause blood pressure changes characteristic for shock. In other animals, anaphylactic shock, upon reinjection of antigen under conditions of hypothermy, is developed with the same intensity as in control animals, with a drop in blood pressure to 10-15 mm (Figure 3).

Figure 3. Drop in blood pressure upon reinjection of antigen against a background of hypothermy (designations as before).

CONCLUSIONS

1. Hypothermy, which occurs following the use of neuroplegic, antihistamine agents and physical cooling, does not prevent the development of hemotransfusion shock in dogs. The additional use of novocain gives analogous results.

2. Reflexes from the baroreceptors are sharply depressed under conditions of hypothermy. The introduction of acetylcholine is accompanied by a less pronounced depressor reaction, but with a more prolonged period of action. The injection of adrenalin and ephedrine gives a hypotensive effect.

3. In some of the sensitized animals, hypothermy prevents the onset of the drop in blood pressure which is typical for anaphylactic shock; in other animals, shock is developed under these conditions.

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II. THE EFFECT OF HYPOTHERMY ON THE MORPHOLOGICAL AND PROTEIN COMPOSITION OF THE BLOOD OF IRRADIATED ANIMALS

[Following is a translation of an article in the Russian-language book *Iskusstvennaya Gipotermiya* (Artifical Hypothermy), Tashkent, State Medical Publishing House, Ministry of Health Uzbek SSR, 1961, pages 21-24.]

Ch. I. Burshteyn, T. G. Mankus, B. I. Kisel', K. A. Shafrina, Sh. I. Rasulev, and Z. N. Karimov, Chair of Pathological Physiology, Tashkent State Medical Institute.

Data on the effect of artificial hypothermy on the development and course of radiation sickness is still contradictory. Information on the status of the functions of the organism irradiated under low body temperature conditions has been only slightly developed.

It is interesting to study the effect of hypothermy on changes in the morphological and protein composition of the blood in irradiated animals, since these indexes characterize the condition of the organism during radiation sickness.

The experiments were performed on rabbits irradiated once with an 800 r dose of x-rays. Hypothermy was produced by neuroplegic and narcotic substances with subsequent physical cooling to a body temperature of 26-28° C.

The animals were divided into three groups. The rabbits in the first group were observed after irradiation and the development of radiation sickness. The animals in the second group were irradiated in the state of artificial cooling. The animals in the third group, observed in a state of artificial cooling, were controls.

First Group of Experiments. In the rabbits irradiated with an 800 r dose, there developed a typical picture of acute radiation sickness with characteristic changes in the peripheral blood (moderately severe anemia with a degenerative blood picture beginning with the 5th-7th day after irradiation and lasting for one month, and leukopenia, already sharply pronounced after 2 hours). Two types of leukocyte reaction were noted within one day: progressing leukopenia in one group of animals, and brief leukocytosis which turned into subsequent leukopenia in the other group. Leukopenia was developed because of a decrease in the number of lymphocytes and neutrophils. The blood composition was not always normalized toward the end of the month.

The protein composition of the blood in the irradiated rabbits underwent the following changes: the total protein content was decreased, most notable on the 5th-7th day, the quantity of albumins was decreased, and the quantity of alpha-, beta-, and gamma-globulin fractions was increased, especially during the first 3 days. The protein composition was gradually normalized over the course of three weeks.

As described in the bulk of published data, shifts in plasma proteins following irradiation reflect complex and severe disturbances in protein metabolism during radiation affection: the phenomena of tissue and blood decomposition, sharp disturbance of vessel and tissue permeability, processes of protein denaturation and the formation of autoantibodies, disturbance of the protein-forming function of the liver. Recently lymphopenia and the increase in globulins connected with it and the decrease in albumins have been treated as a manifestation of one of the phases of the adaptation syndrome (the catabolism phase).

Second Group of Experiments. Changes in the morphological composition of the blood, which also occurred in the foregoing experiments, occurred in animals irradiated in a state of hypothermy at a body temperature of 28° C. But in several rabbits, normalization in comparison with the controls required a longer period (up to 3 months), and a second wave of anemia and leukopenia occurred within 2-3 months.

The dynamics of the total protein and albumins was the same as that in rabbits of the preceding series, but the decrease in their content during the first day was more pronounced. A more significant increase in the content of alpha- and beta-globulin fractions was noted during the first 3 days. It should be noted that this very increase in the content of these fractions is considered an index of denaturation changes in the plasma proteins.

Our attention was turned to the uninterrupted decrease in gamma-globulin fraction during the entire period of the investigation, which possibly attests to the inhibitability of the reticuloendothelial system and to disturbances in the immunobiological properties of the organism in the experiments as set up.

Control Group of Experiments (animals subjected to hypothermy). The morphological and protein composition of the blood of cooled animals was altered most essentially during the first 72 hours after cooling. The percent of hemoglobin and the quantity of leukocytes were decreased primarily because of the lymphocytes, mainly at the time of deep hypothermy and 2 hours after its occurrance.

Analogous data were obtained in the laboratory of N. N. Sitotinin.

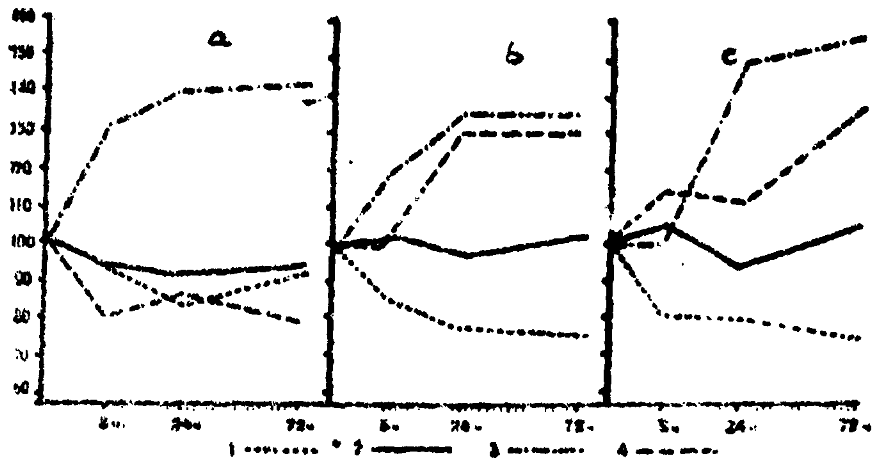
There are indications in the literature of a redistributing mechanism of this leukopenia, connected with circulatory disturbances and an increase in vascular permeability.

O. Miletzky, J. Rienau, and J. Espagno (1955) considered that the leuko-lymphopenia indicates an overstrain of the hypophyseal-adrenal system during artificial cooling. We are inclined to connect the leukopenia with an observed (in our laboratory) thinning of the blood after the introduction of aminazine.

A decrease in the content of total protein and albumins, also probably connected with thinning of the blood, was noted in the protein composition of the blood. Toward the 72nd hour, all indexes, with the exception of the alpha-globulin fraction, are returned to normal level; the albumin content remains low up to the 5th-7th day after cooling. This is explained, possibly, by the long period of after-effects in the disturbance of protein synthesis following artificial cooling (V. I. Nikulin). Our attention was drawn to the notable increase in the alpha-globulin fraction also observed by other authors (Ye. D. Ponomareva, T. I. Dzhaparidze). P. Ottavioli, B. Venejoul, and H. de Metroe, noting the connection of the alpha-globulin fraction with lipoproteins, consider its increase an expression of the mobilization of the hypophyseal system with a deposition of adrenal steroid hormones in the blood.

The aforementioned changes (see illustration) in protein fractions during the first 72 hours are clearly seen upon comparison of the blood picture data in all those series in percentages from the initial.

The impression is created that a combination of hypothermy and irradiation gives a summation of shifts characteristic for both conditions--a more pronounced drop in the content of total protein and albumins in the first days, and a higher rise in beta-globulins (by 37%) and especially in alpha-globulins (by 54%) than following irradiation alone.



The dynamics of protein fractions in the first 72 hours:

a - hypothermy; b - irradiation; c - hypothermy plus irradiation.

1 - albumin; 2 - total protein; 3 - alpha-globulin; 4 - beta-globulin.

N. N. Sirotinin formulated a general opinion when he stated that hypothermy has a greater effect on the initiation of pathological processes than on their course.

Not interrupting the development of the radiation syndrome, cooling in our experiments did not normalize the morphological and protein composition of the blood of irradiated animals.

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