SOME PECULARITIES OF ANEMIAS INDUCED BY DENERVATION OF THE CAROTID SINUSES AND AORTA

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In the eighties of the last century the outstanding Russian therapist, S. P. Botkin, on the basis of his clinical observations, postulated a theory of the existence of a nervous regulation of blood formation. Since that time, the problem of the nervous influence on blood formation has occupied the attention of a number of investigators in our country.

The work of I. P. Pavlov and co-workers led to the establishment of the Pavlovian school in physiology, which afforded an opportunity of a new approach to the study of the question of a nervous regulation of the blood system.

Recently, this problem has been developed in the works of B. I. Bayandurov, G. S. Belenky, M. L. Belenky and Yu. N. Stroikovy, V. A. Beier, V. G. Vogralik, D. I. Goldberg, N. S. Dzhavadyan et al. [2, 3, 4, 6, 7, 8].

A series of experimental anemias was obtained and studied by E. L. Kan after denervation of the spleen, by O. I. Moiseev after partial denervation of the liver, by S. I. Yakovlev, after denervation of the pit and body of the stomach, by A. Ya. Yaroshevsky [12] after denervation of the carotid sinuses and aorta, and by other workers. The results of these investigations have been generalized by V. N. Chernigovsky and A. Ya. Yaroshevsky [10].

The anemias induced by these authors while having features in common are characterized by a number of differences. Of definite interest in this connection is the question of whether these anemias, arising after denervation of the various internal organs (stomach, intestines, spleen, carotid and aortal receptors), are specific, or whether they constitute a common reaction of the blood system to denervation of the various organs and receptor zones.

The object of our investigation was to study the characteristic features of anemia produced by denervation of the carotid sinuses and a transverse cut of the depressor nerves.

EXPERIMENTAL METHOD

Long-term experiments were conducted on 8 rabbits. At the same time blood investigations were conducted on 6 control rabbits.

The following indications were determined in all the animals: erythrocyte count, percentage of hemoglobin (Sahli's method), number of leucocytes and reticulocytes, the osmotic resistance of the erythrocytes, the volume of the erythocytes (hematocrit), the diameter of the erythrocytes (animocytosis, poikilocytosis, polychromatophilia), and also the punctates of the bone marrow. In addition, in two of the rabbits a study was made of the amount of bilirubin (according to Huymans-van den Bergh) [1], and of plasma iron values (according to Barkan-Walker) [1].

The blood indices were studied for 3-4 weeks before operation. Following operation blood was taken daily from a prick in the ear lobe, and as from the third month every 3-4 days. The investigation continued for seven months.

Denervation was carried out in the following manner: the carotid sinuses were prepared and the carotid gland destroyed and after carefully removing the adventitia around the sinus, this region was smeared with 10% solution of phenol. Resection of the depressor nerves was then performed. The extent of denervation was verified later in acute experiments (hypertension and absence of carotid reflexes). In the control animals the operation consisted in preparing the carotid sinus and depressor nerves. The cervical muscles in the controls were smeared with 10% solution of phenol.

EXPERIMENTAL RESULTS

Before the operation fluctuations in the blood indices in all animals were insignificant (Graphs 1 and 2, left of arrow).

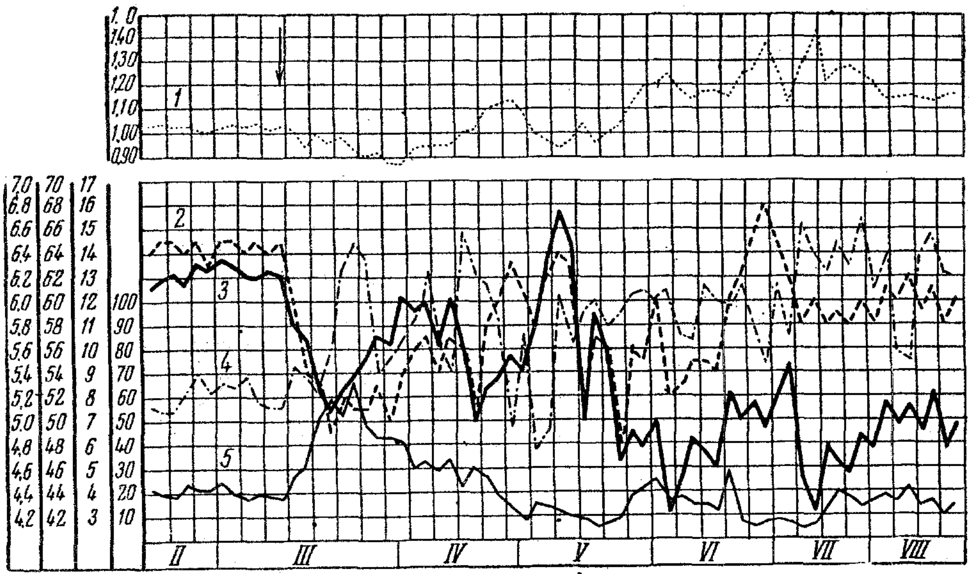

Fig. 1. Dynamic of the changes in blood composition with denervation of the carotid sinuses and aorta in a rabbit.
Curves: 1) Color index, 2) hemoglobin, 3) erythrocytes, 4) leucocytes, 5) reticulocytes. Operation indicated by arrow(↓).

As a result of denervation, a sharp change in all the blood indices was noted within the first few days. The maximum change occurred from the 10-17th days, the number of erythrocytes decreased by more than 1,000,000; the hemoglobin fell by 12-15%. The number of leucocytes increased by 6,000-7,000 and the reticulocytes three- to fourfold (Fig. 1). At the peak of the reticulocyte crisis a significant increase in the most immature reticulocytes (coarse cells) was observed. Simultaneously there occurred a significant increase in the number of polychromatophils, a manifestation of a marked poikilocytosis and anisocytosis. The diameter of the erythrocytes was reduced, that is, the erythrocyt-metric curve shifted to the left (Fig. 3). In punctates of the bone marrow a perceptible intensification of erythropoiesis was observed (increase in the number of reticulocytes, erythroblasts II and particularly of erythroblasts III, and a significant increase in mitoses (see Table).

Hypochromia was disclosed in color index findings of the blood. At the height of the anemic wave the minimum resistance of the erythrocytes fell and there was a significant increase in the maximum resistance (see Fig. 3,a). The fall in the minimum resistance of the erythrocytes was obviously connected with the intensification of the hemolytic role of the spleen following denervation. However, the increase in the maximum

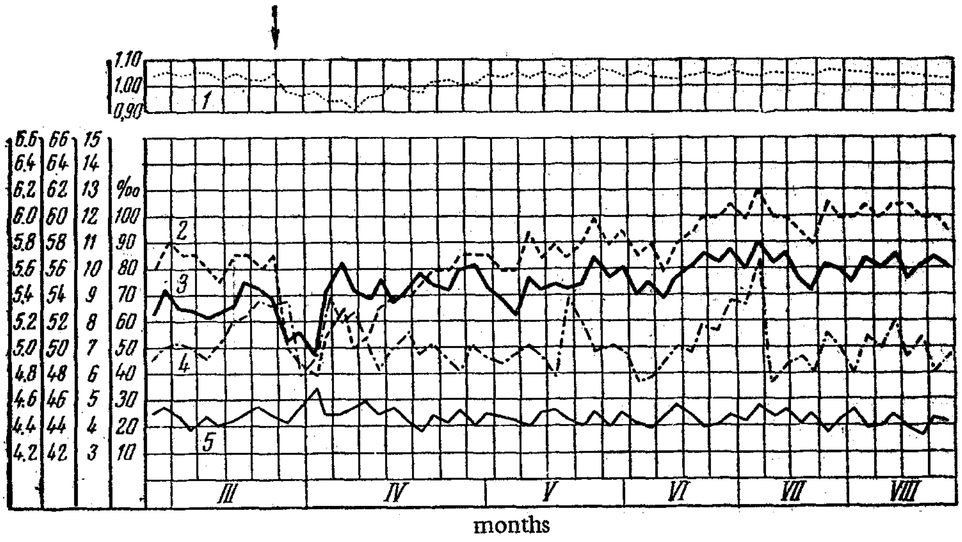

Fig. 2. Dynamic of the changes in blood composition after operation on neck of control rabbit No. 6.
Curves denoted as in Fig. 1.

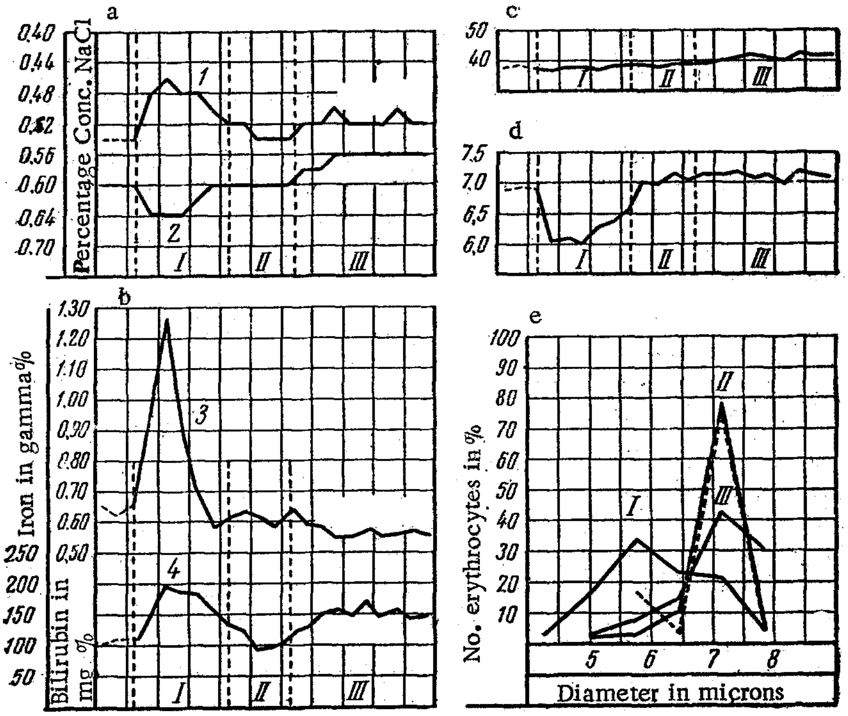

Fig. 3. Characteristic curves of the blood picture after denervation of the carotid sinuses and aorta in rabbit No. 3.
a) Osmotic resistance of the erythrocytes; 1) maximum, 2) minimum; b) bilirubin content (3) and iron content (4); c) hematocrit index; d) average diameter of erythrocytes in μ; e) erythrocyt-metric curve: I, II, III) waves of anemia, dotted line, before operation, unbroken line, after operation.

Changes in the Myleogram (Erythropoiesis) After Denervation of the Carotid Sinuses And Tranverse Incisions of the Depressor Nerves in Rabbit No. 3 (in percentage)

Time of puncture	Mitoses	Erythroblasts			Reticulo-cytes
		Type I	Type II	Type III	
Before operation	0.4	8.2	17.6	14.0	2.7
First wave	1.8	4.3	19.2	21.4	7.7
Second wave	0.6	10.9	15.0	11.8	3.2
Third wave	0.2	11.3	14.6	10.1	1.3

resistance indicates that alongside a drecrease in resistance of the general mass of erythrocytes in the peripheral blood there appeared erythrocytes with a greater resistance than before denervation. The increase in the maximum resistance must be attributed to the large increase in the number of reticulocytes and polychromatophils since the young forms of the erythrocytes, as is known, are more resistant [6, 7]. According to hematological data, the increase in maximum resistance with simultaneous reduction in minimum resistance is characteristic of hemolytic anemia [11]. This is also indicated by the volumetric estimation of erythrocytes. While the diameter of the erythrocytes was reduced, the hemocrit remained almost unchanged, that is, microspherocytosis occurred also, a characteristic of hemolytic anemia.

The amount of bilirubin at the height of the anemia more than doubled, and then swiftly returned to the original level. The easily separated iron also rose almost double and then slowly fell back to the original level (Fig. 3).

Thus, the anemia which developed in the first two weeks after denervation was a hemolytic, microcytic, hypochromic anemia of the regenerative type. Approximately one month after denervation all the blood indices approached the original values, but on the 40-45th day there occurred a second change in the blood indices. Unlike the first anemic wave, this time the number of reticulocytes did not increase, which bore witness to a weakening of the regenerative function of the bone marrow (see Fig. 1). In the punctates of the bone marrow a suppression of erythropoiesis was observed.

The number of forms of division of the erythroblastic series (mitoses) proved to be significantly less than before; the number of erythroblasts of Type II and III fell and there was a relative increase in the number of erythroblasts of Type I (see Table). The osmotic resistance did not change. Bilirubin and iron values remained at the previous level. On the 65-75th day the blood indices returned to the original values.

On the 75-85th day there occurred a third, even sharper change in the blood indices. The number of erythrocytes fell by 2,500,000 and the amount of hemoglobin by 10-12%. The number of leucocytes increased by 3,000-5,000 and then remained constant at a high level.

The number of reticulocytes was less than the original number, although at times insignificant rises were observed.

Also characteristic were the large sweeps in the fluctuations in the number of the formed elements and hemoglobin. The hemoglobin value at first fell and the color index was more than unity (see Fig. 1). The osmotic resistance of the erythrocytes rose, the minimum resistance in particular. The diameter of the erythrocytes during the second and particularly during the third wave was somewhat larger than originally. During the 2nd and 3rd phases the hemocrit value increased. The amount of bilirubin was less than the original amount and the iron value again increased (see Fig. 1). This anemic wave continued for about 90 days. However, during that time the blood picture did not return to its original values.

Thus, the second and particularly the third wave of anemia differed from the first by their depth and duration and also by a number of characteristic features: high color index, absence of reticulocytosis, suppression of erythropoiesis, insignificant changes in osmotic resistance, increased cell diameter and volume of erythrocytes, a certain reduction in the bilirubin content and an increased iron value. On the basis of all this one can assume that here the participation of the hemolytic influence of the spleen in the anemic process was not marked, the cause of the anemia process being a perceptible weakening of hemopoiesis in the bonemarrow. The second and third anemia waves resembled a hyperchromic, normocytic anemia of the hyporegenerative type.

In the control rabbits immediately after operation anemia of short duration occurred. The maximum change was on the 5-8th day. The number of formed elements decreased insignificantly (Fig. 2). The minimum resistance declined and the maximum rose somewhat. The hemocrit value did not change. In the punctates of the bone marrow an insignificant increase of erythropoiesis was observed. The color index was less than unity. After 10-14 days all the indices returned to the original levels, and within the next five months fluctuated within the limits of the original values. Thus, in the control rabbits there occurred, after operation, an insignificant, short duration, hemolytic, hypochromic anemia of the regenerative type. Thus, the development of the wave-like anemias after denervation of the carotid sinuses and the aorta testify to the presence of a functional reflex connection between the given receptor zones and the organs of the blood system (spleen, bone marrow, etc.).

There are references in the literature to the close reflex connection between carotid sinuses and the spleen [12]. Obviously, there normally exists a constant tonicizing impulsion from the receptors under discussion to the central nervous system, and from there to the corresponding organs of the blood system. Such an impulsion contributes to the maintenance of a constant level of activity of the organs of the blood system by which the relative consistency of the composition of the circulating blood is ensured. A stimulus for these receptors is the changes in the degree of oxygen saturation of the arterial blood, which is closely linked to the number of erythrocytes and the hemoglobin contained in them. Consequently the number of erythrocytes and hemoglobin act indirectly as a reagent for the peripheral receptors and hence control the level of activity of the organs through the nervous system.

The destruction of such a connection after denervation leads to a disturbance in the activity of the organs of the blood system. As a result of denervation the activity of the organs of the blood system at first is intensified; this change, however, chiefly affects the spleen and, to a lesser degree, the bone marrow. There is a considerable intensification of the hemolyzing role of the spleen, and although the activity of the bone marrow increases, it is insufficient to compensate for the rapid destruction of the erythrocytes, with resulting anemia. Hence the correclation in the activity of the spleen and bone marrow is disturbed, i.e., between blood destruction and blood formation.

During the second and third waves of anemia, there occurs a weakening in the activity of the organs of the blood system. In the given case the anemia was chiefly related to the suppression of erythropoeisis in the bone marrow, that is, in the subsequent stages of denervation the bone marrow is principally affected

As is known, the spleen is considered as the organ regulating hemopoeisis [5]. Therefore the suppression of the activity of the bone marrow can be explained both by a disturbance of the regulating influence of the spleen on hemopoeisis as a result of denervation of the carotid sinuses and aorta, and by a disturbance of the reflex connection of the central nervous system between the carotid and the aortic receptors and the bone marrow.

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