CHARACTERISTICS OF THE ANEMIA FOLLOWING DIVISION OF THE VAGUS NERVES

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The problem of the nervous regulation of the blood system has recently attracted the attention of many researcher. Much factual material has been collected and analyzed [1-4, 8, 9].

V. N. Chernigovskii and his co-workers have studied and described experimental anemias caused by denervation of certain internal organs [4,8,9]. In these investigations an important place is occupied by the study of the anemias arising as the result of partial denervation of the stomach by the formation of a gastric pouch by the Klemenciewicz-Heidenhain method [2,4,9].

In the present article we describe an experimental anemia caused by the bilateral subphrenic division of the vagus nerves.

METHOD

Experiments of long duration were performed on 3 experimental and 2 control dogs. The blood indices examined in all the dogs before and after operation included cell count, hemoglobin concentration, osmotic resistance, diameter and volume of the red cells (hematocrit), and examination of bone marrow films. We also studied the uptake of radioactive iron Fe^{59} by the red cells and made a morphological analysis of the gastric mucosa. The operation was performed under general ether anesthesia. Both vagus nerves were divided below the diaphragm, an annular strip of the mucous membrane was removed from the cardial portion of the stomach, and this area was then painted with a 10% solution of phenol. The control operation consisted of dissection of the vagus nerves in the cardial portion of the stomach. The surrounding tissues were painted with the same phenol solution. Before operation, and during the first 3 months after the operation, blood examinations were made on alternate days, and subsequently once every 3-4 days. The investigations lasted 10 months.

RESULTS

In Fig. 1 are shown the changes in the peripheral blood of the control dog Belyak. We can see that during the 5 months before operation the variations in the cell counts and the hemoglobin concentration were insignificant. The osmotic resistance, diameter and volume of the red cells, and also the bone marrow picture, remained stable.

Radioactive iron Fe^{59} was found in the plasma 15-30 minutes after its administration, reached its maximum level after 120-240 minutes, and then began to fall off in concentration. Radioactivity was detected in the red cells on the 4th-5th day, reaching its maximum on the 8th-9th day, at which level it stayed for a long time, and then gradually decreased in intensity. After 4 months the Fe^{59} content of the red cells did not exceed 1%*.

After the control operation, the dog Belyak developed a transient hypochromic anemia. On the 5th day the red cell count fell by 900,000 and the hemoglobin level by 12%; the reticulocyte count increased fourfold. The remaining blood indices were unchanged. On the 10th day the number of red cells and reticulocytes and the hemoglobin percentage returned to their initial values (see Fig. 1). After the repeated administration of radioactive iron we obtained the same results. The changes which have been described were also obtained in the other control dog, Malysh.

More siginificant and lasting changes were observed in the blood picture and the bone marrow after division of the vagus nerves. In the dog Bars (Fig. 2), for instance, on the 10th day after division of the vagus nerves the red cell count fell by 2,000,000; the hemoglobin concentration at first rose, but by the 17th day it had fallen by 16% of its initial value; the white cell count rose sharply in the first few days, but gradually returned to its initial level; in the same period there was a threefold increase in the reticulocyte count, but at the end of the first month it returned to its initial value. At the beginning of the second month the red cell count rose, and was now 1,000,000-1,200,000 below its normal value.

*Byull. Eksptl. Biol. i Med. 3, 51-55 (1958); see CB translation.

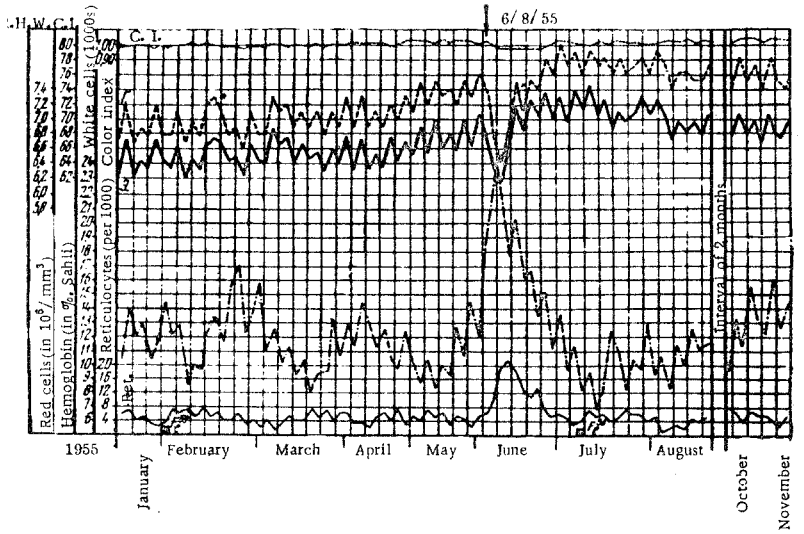

Fig. 1. Changes in the peripheral blood in the control dog Belyak. The arrow indicates the operation. The black squares denote times of radioactive iron administration.

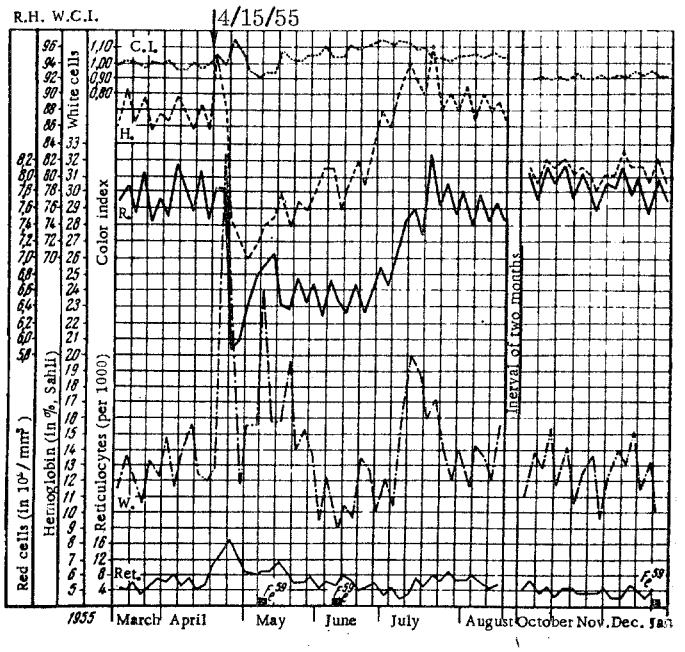

Fig. 2. Changes in the peripheral blood of the experimental dog Bars after subphrenic division of the vagus nerves.

The hemoglobin percentage rose rather more quickly, so that the color index was greater then unity. At this period the anemia was thus hyperchromic in character. The osmotic resistance of the red cells, especially the maximum value, increased appreciably. The mean red cell diameter increased by 0.8μ and a significant anisocytosis developed (Fig. 3). The findings of investigation of the bone marrow are shown in the table. They indicate that some degree of depression of erythropoiesis was observed at this period.

On two occasions, at the end of the first and second months after operation, this dog received radioactive iron (see Fig. 2). In contrast to the control animals the radioactivity of the plasma was reduced to one quarter, and on the following days no traces of Fe^{59} could be detected. Radioactivity was found in the red cells on the 3rd-5th day, reaching its maximum on the 6th-7th day, but its level was much lower. Despite the development of anemia, the utilization of radioactive iron in the experimental dog was thus sharply diminished by comparison with its utilization in the control dogs. It was found that 88% of the administered iron was excreted with the feces. At the end of the 3rd month the red cell count and the hemoglobin concentration had almost returned to their initial values. At this period the color index gradually fell. The changes in the osmotic resistance and diameter remained as before. The intensity of erythropoiesis was restored (see table).

Six months after operation the red cell count was at its initial level, but the hemoglobin concentration was reduced by 10-12% and the color index was now 0.9. The hemoglobin saturation index of the red cells, obtained by calculation [5], was considerably reduced (see Fig. 3). The osmotic resistance and diameter of the red cells remained as before.

In the course of the next three months the blood picture remained unchanged from that described. At the end of the investigation, radioactive iron was given on three occasions, and the same results were again obtained.

In the other two dogs, Tarzan and Fokus, the blood changes after operation were identical in character. Bilateral subphrenic division of the vagus nerves led to the development of a hyperchromic macrocytic anemia with signs of depression of erythropoiesis.

Six months after operation the red cell count had returned to its initial level, the intensity of erythropoiesis was restored and the anemia as such was corrected, although certain qualitative changes persisted. The decreased percentage of hemoglobin, the lowered hemoglobin saturation index of the red cells and the sharp fall in the utilization of radioactive iron evidently indicate some depression of the process of hemoglobinization of the red cells at a later period after operation.

According to findings obtained by V. A. Samtsov [7] and S. I. Yakovlev [9], after division of the vagus

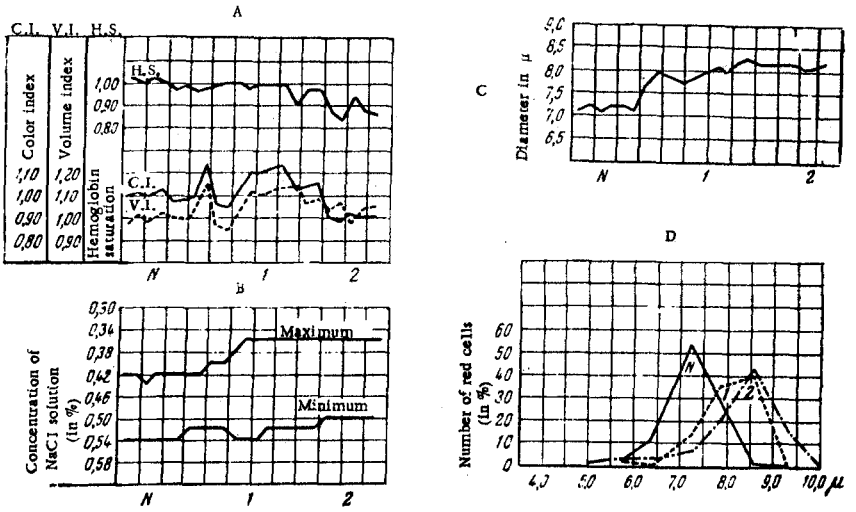

Fig. 3. Characteristic curves of the blood picture in the dog Bars after subphrenic division of the vagus nerves. A) Index of saturation of the red cells with hemoglobin (H.S.); B) osmotic resistance of the red cells (maximum and minimum); C) mean red cell diameter; D) erythrocytometric curve; N) before operation; 1,2) periods of anemia; V.I.) volume index.

Changes in Erythropoiesis in the Bone Marrow after Subphrenic Division of the Vagus Nerves in the Dogs Bars and Fokus

Periods of investigation	Date of investigation	Number of dividing forms (mitoses)	Erythroblasts	Pronormoblasts	Normoblasts: basophilic	Normoblasts: polychromatophilic	Normoblasts: orthochromatic	Reticulocytes	Red cell count in the peripheral blood (in 10^3/mm^3)
		as a percentage of 100 bone marrow cells							
Bars									
Before operation	7/IV	0.1	0.5	1.8	5.7	10.3	15.2	0.7	7940
After division of the vagus nerves	5/27	0.3	0.9	2.4	4.3	8.7	11.9	0.7	6450
The same	7/27	0.2	0.6	2.1	5.4	10.4	14.7	1.1	7540
" "	12/24	0.1	0.6	1.7	6.1	10.1	15.5	0.8	7940
Fokus									
Before operation	4/7	—	0.7	1.7	6.2	11.6	14.7	0.5	7610
After division of the vagus nerves	5/6	0.3	1.1	2.5	4.7	9.9	12.9	2.1	6325
The same	7/26	0.1	0.6	1.9	5.7	11.2	15.2	0.7	6940
" "	7/21	0.2	0.8	1.8	6.4	11.9	15.4	0.5	7465

nerves in dogs, the antianemic activity of the gastric juice is sharply decreased. The morphological analysis which we undertook showed that after division of the vagus nerves the gastric mucosa undergoes a series of characteristic changes, testifying to disturbances of the nutrition of this area. The changes were seen especially clearly in the intramural nervous system of the stomach. Areas with complete degeneration of the intramural nerve cells were seen, in which only the cell membranes were preserved, here and there with pyknotic nuclei, waxy accumulations of myelin, and so on. Similar findings were published by E. A. Rudik [6].

So far as the blood system is concerned, the results of division of the vagus nerves was th. the development of a hyperchromic anemia, and —in the stomach itself — trophic disturbances and degeneration of the intramural nerve cells and apparatus. The latter may lead to a disturbance of the synthesis of antianemic factor in the gastric mucosa and may be the cause of development of the anemia which was observed.

In our opinion, however, the decrease in the antianemic activity of the gastric juice could hardly cause the development of anemia. Besides the stomach, the duodenum and small intestine are known to possess considerable antianemic activity. From the foregoing it may be postulated that production of antianemic factor is disturbed not only in the stomach, but also in the remaining part of the digestive tract.

Division of the vagus nerves involves destruction of both the efferent and afferent connections of the stomach with the central nervous system. The abolition of afferent impulses from such an extensive receptor region as the stomach may lead to failure of information and to disturbance of the central nervous mechanisms regulating the blood system. This explanation is based on V. N. Chernigovskii's hypothesis [8] of the great importance of constant tonic impulses, passing from the internal organs to the central nervous system, in the maintenance of the constancy of the blood system.

The disturbances which we observed are, of course, functional in character. The diminished red cell count is gradually restored and the anemia as a rule is corrected.

The sharp disturbance of utilization of radioactive iron, and the slight lowering of the hemoglobin concentration and the hemoglobin saturation index of the red cells however, are evidence that qualitatively more delicate and complicated processes such as hemoglobinization of the red cells suffer more from denervation than do quantitative processes, which are more independent, such as the proliferation and development of erythroid tissue. In this connection it may also be suggested that the cessation of afferent impulses from the stomach to the central nervous system leads not only to disturbance of efferent influences on the processes of synthesis of the antianemic factor in the alimentary tract, but also to disturbance of direct efferent influences on the bone marrow tissue.

SUMMARY

The author studied the effect of bilateral subdiaphragmatic division of the vagus nerves on the blood system in chronic experiments on dogs.

The development of hyperchromic macrocytic anemia lasting for a period of 3 months was noted. Sharp reduction in the utilization of radioactive iron (Fe^{59}) was found together with degenerative and trophic disturbances in the gastric mucosa. Later, the red cells recovered their normal level.

A relatively low hemoglobin percentage and disturbed radioactive iron utilization lasted up to the end of the investigation (10 months). Some mechanisms of disturbances observed in the blood system are discussed.

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