CHANGES IN THE BLOOD SYSTEM ASSOCIATED WITH DENERVATION OF THE DUODENUM

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S. P. Botkin [1] was the first to recognize the possibility that the stomach, and, in particular, the duodenum, act reflexly on the composition of the blood. Presently there is no doubt about the close functional relationship between the organs of the digestive tract and the blood system. It has been shown, by a number of investigations [2, 3, 6, 8, 9, 11], that significant changes occur in the peripheral blood and bone marrow pictures as a result of either the removal of various portions of the digestive tract or the exposure of its mucosa to certain influences. These influencing factors often lead to the development of anemia. Reflex changes in the blood composition, in association with a diverse number of actions on the duodenal receptor apparatus, have been established as plausible [4, 5, 7, 8]. In our opinion, these observations testify to the importance, in the regulation of the blood system, of the efferent impulsation, and, in particular, the afferent impulsation, traveling from the receptor field of the duodenum.

In this investigation, we used the denervation method to exclude innervation and to exclude the afferent impulses in particular in order to study the effect of denervation of the duodenum on the blood system.

EXPERIMENTAL METHODS

The investigations were carried out as a chronic experiment on eight male cats; parellel investigations were conducted on the blood of six control cats. In each animal, the number of erythrocytes, leukocytes and reticulocytes, the percentage of hemoglobin, the osmotic resistance (fragility) of the erythrocytes, the volume of erythrocytes (hematocrit) and the average erythrocyte diameter were determined. The red marrow picture was studied in a few of the animals. The indices of the blood were studied for 3-4 weeks before the operation. Blood was taken from a small incision in the ear every other day until the third month after the start of the experiment, when it was taken every 3-4 days. Bone marrow was taken from the region of the upper third of the tibia while the animal was under general ether anesthesia. The investigations lasted 5-8 months. Denervation was performed as follows: all nerves terminating in the neu-

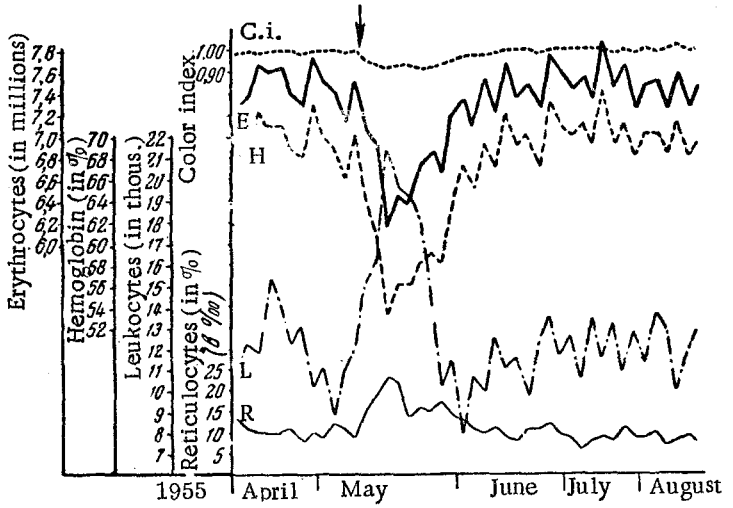

Fig. 1. Change in the peripheral blood after the control operation. E) Erythrocytes; H) hemoglobin; L) leukocytes; R) reticulocytes; C.i.) color index. Arrow shows the time of the operation.

rovascular bundle and going to the duodenum were cut; the adventitia was carefully removed from the vessels, which were then smeared with a 10% phenol solution. A layer of the serous membrane was annularly resected from the region where the pylorus meets the duodenum, and this section was also smeared with the 10% phenol solution. The control operation involved dissecting out the vessels and nerves of the same region.

EXPERIMENTAL RESULTS

The fluctuations in the blood indices of all the animals were slight before the operation (Fig. 1 and 2, to left of arrow).

The development of slight, short-lived anemia of the hyperchromic type, lasting 3-4 weeks, was observed after the control operation. All the blood indices returned to the original figures about the end of the first month and did not subsequently undergo any further change (see Fig. 1).

Substantial and considerable changes in the composition of the blood and bone marrow occurred after denervation of the duodenum. On the 2nd-3rd day after the operation, the erythrocytes increased 600,000-900,000 in number, but then decreased sharply on the 4th-8th day—by almost 2-3 million. Then, despite great fluctuations, the number of erythrocytes began to increase, in some cases even reaching the normal minimum; this period lasted 20-50 days, after which the number of erythrocytes began to decrease, variably but steadily, until at the end of the investigation their deficit constituted 2-2.5 million.

The changes in the hemoglobin content reflected those in the number of erythrocytes, but the decrease in the hemoglobin percent was less marked; the color index, therefore, began to increase gradually, and the initial hypochromic anemia was superceded by hyperchromic anemia (see Fig. 2). After the denervation, the number of reticulocytes increased from 9 to 30‰, and a shift of the reticulocytes to the left was observed. Towards the end of the second month, during the second decrease in the number of erythrocytes, the content of reticulocytes returned to the original level and subsequently remained fairly stable (see Fig. 2).

The osmotic resistance of the erythrocytes changed during the first period (minimal decreased 0.06%, maximal increased 0.04%), then returned to the original level (Fig. 3). The average erythrocyte diameter first decreased from 5.5 to 5μ, then gradually increased to 6.2μ (see Fig. 3). Characteristic changes occurred in the size and shape of the erythrocytes: during the initial period following denervation, the average volume and area of the erythrocytes decreased; the cells became thicker and microspherocytic in shape; then, during the period in which the development of hyperchromic anemia was observed, the average volume and area of the erythrocytes increased, the thickness diminished, and the cells took the form of macroplanocytes. The erythrocytometric curve also changed. The index of erythrocyte hemoglobin saturation decreased considerably (see Fig. 3).

The changes in the erythroid primordium of the bone marrow are described by the data presented in the Table, which show that erythropoiesis became inhibited after the denervation. This general retardation of erythropoiesis was attened by disturbance of the maturation process in stabe II of erythropoiesis. Therefore, denervation of the duodenum led to the development of anemia with a characteristic oscillation course.

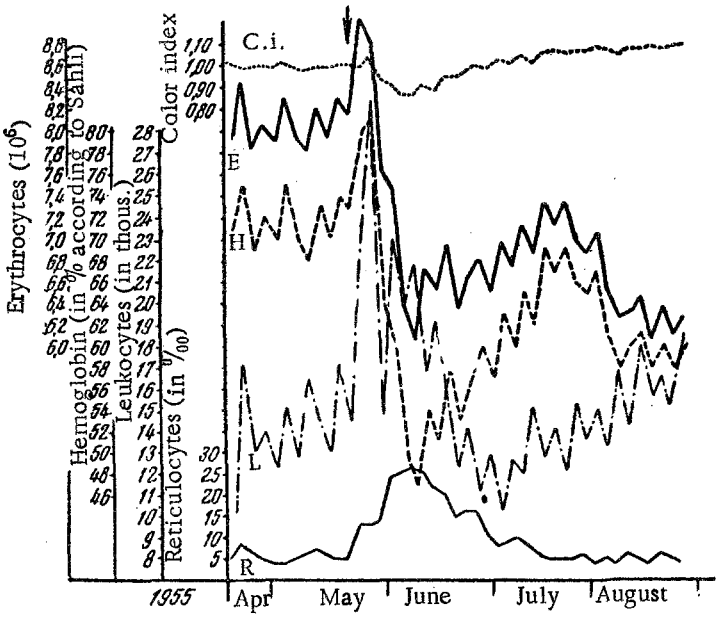

Fig. 2. Change in the peripheral blood after denervation of the duodenum. Symbols the same as in Fig. 1.

Change in Erythroid Primordium of Bone Marrow after Denervation of Duodenum (in % of 100 Bone Marrow Cells)

No. of experimental animal	Examination date*	Examination period	No. of dividing forms (mitoses)	Erythroblasts	Pronormoblasts	Normoblasts: basophilic	Normoblasts: polychromatophilic	Normoblasts: orthochromic	Reticulocytes	Number of erythrocytes in the peripheral blood
17	May 18	Bef. oper.	0.2	0.7	1.4	6.3	13.4	17.0	1.1	7 980 000
	Aug. 12	Aft. dener.	—	1.2	1.9	4.5	10.0	10.8	0.6	5 840 000
18	May 14	Bef. oper.	0.3	0.6	1.1	5.1	11.3	15.7	0.9	7 660 000
	Aug. 4	Aft. dener.	0.2	1.0	1.3	5.7	9.6	13.1	1.0	5 190 000
	Nov. 28		—	1.3	1.9	4.2	8.1	9.0	0.6	6 000 000
20	May 7	Bef. oper.	0.4	0.7	1.3	5.8	13.7	16.9	0.9	7 240 000
	Aug. 8	Aft. dener.	—	1.3	2.2	3.6	11.2	11.7	0.6	5 710 000

*All investigations conducted in 1955.

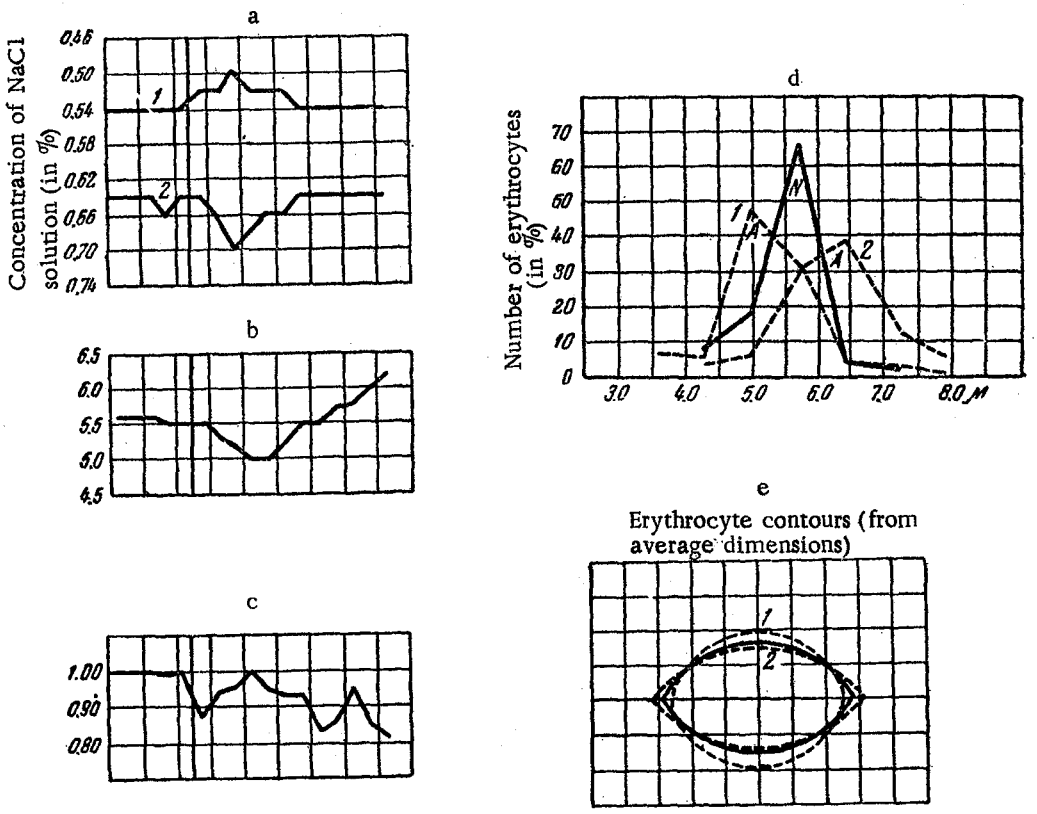

Fig. 3. Characteristic curves of the blood picture after denervation of the duodenum. a) Osmotic resistance of erythrocytes (1-maximal, 2-minimal); b) average erythrocyte diameter (in microns); c) index of erythrocyte hemoglobin saturation; d) erythrocytometric curve (N-before operation, A-during anemia); e) schematic shape of erythrocytes (according to average dimensions); 1-first wave of anemia, 2 -second wave of anemia.

During the first month following the operation, hypochromic, microcytic anemia of the regenerative type developed. Then hyperchromic, macrocytic anemia of the hyporegenerative type developed. The biphasic character of the anemia indicates diverse causes of its development. The first wave of anemia, hypochromic and microcytic in nature, was attended by marked reticulocytosis, a shift of the red blood to the left and great leukocytosis. Microspherocytosis and typical changes in the osmotic resistance were observed. All these changes developed under conditions of active erythropoiesis and were very typical of the hemolytic form of anemia. Similar, but less pronounced, changes were observed after the control operation. It would therefore appear that the initial mechanism of development of the anemia was the same with both denervation and the control operation and was caused by intensified hemolysis of the blood.

What are the reasons for intensified hemolysis? Every operative intervention is to some extent an injurious factor to begin with. The tissue in the vicinity of the denervation becomes a focus of intensified afferent impulsation, which produces a state of excitation in the central nervous system, and this, in turn, increases the activity of other systems, the blood system included (active erythropoiesis, reticulocytosis, leukocytosis). The intensification of the hemolytic processes is evidently stronger than that of the hemopoietic [5]. The spleen, which as the most labile organ in the blood system is considerably more sensitive to nervous influences, is irritated to a greater extent than the bone marrow tissue. It should be realized, however, that this mechanism cannot continue for long periods. The traumatic sequelae pass, and the original composition of the blood is restored. We believe this to be the mechanism of development of the anemia observed during the initial period after the operation.

Denervation stops the constant tonicizing impulsation from the intestinal receptors to the central nervous system and interrupts the efferent impulses. This diminishes the activity of the central nervous system apparatuses and weakens their inhibitory influence so that the blood system is, in a manner of speaking, "disinhibited" [8]. Under these conditions, the hemolytic function of the spleen is evidently intensified [5]. Of course, the disturbances induced in the central nervous system are not confined to the above.

The more or less identical character of the changes in the blood and bone marrow pictures after the control operation and during the initial period following denervation of the duodenum gives reason to believe that these changes were general in nature and cannot be considered to be specifically associated with denervation of the given organ. However, qualitatively new changes occurred soon after the first wave of anemia ended: a second, more stable and pronounced wave developed, this time of hyperchromic macrocytic anemia of the hyporegenerative type. There were no signs of hemolysis, and a low level of hematopoiesis was typical (see table). This could have been due to disturbance of the relevant efferent influences on the mucosa of the digestive tract from the central nervous system [8]. Disturbance of the relevant humoral mechanisms is also possible [10]. Therefore, during the second phase of development of anemia in the blood system, qualitatively new changes occurred which can be considered to be specific, associated with denervation of the duodenum.

SUMMARY

The effect of duodenal denervation upon the blood system was studied in conditions of chronic experiment (5-6 months) in 8 male cats. Six control male cats were investigated simultaneously. Two waves of anemia development were observed: the first—hypochromic, microcytic anemia of regenerative type; the second—hyperchromic, macrocytic anemia of hyporegenerative type. Some possible mechanisms of biphasic anemia development are discussed.

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