THE CHARACTER OF EXPERIMENTAL ANEMIAS CAUSED BY DENERVATING VARIOUS SECTIONS OF THE DIGESTIVE TRACT

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The existence of a close functional link between the organs of the alimentary canal and the blood system is widely recognized today. It has been shown that the exclusion of the gastrointestinal tract receptors and influences on them changes the composition of the blood [1,2,3,4,5,10,12]. The studies establishing the development of anemia due to denervation of certain internal organs are especially interesting [5,6,7,8,10,11].

The purpose of our work was to study the general and specific pictures of anemias caused by denervating the caudal section of the small intestine, the duodenum and a portion of the stomach.

EXPERIMENTAL METHODS

Cats and dogs (males) were studied as long-term experiment. One group was used as the control and in the experimental animals, one of the above organs was denervated. The amount of erythrocytes, hemoglobin, leukocytes, reticulocytes, osmotic fragility and the average diameter of the erythrocytes and the hematocrit index were determined in all of the animals. Bone marrow punctates were examined in some of the animals. The amount of bilirubin and easily-liberated iron were also determined in the dogs, and studies were done with labeled iron.

All the operations were performed under general ether anesthesia. When denervating the duodenum and the caudal section of the small intestine, all the nerves running through the part in question were resected. The adventitia was also removed from the vessels, and the vascular walls were coated with a 10% phenol solution.

The stomach was denervated by forming a pouch according to Klementsievich and Heidenhain's method (of the usual size), thus denervating the bottom and part of the body of the stomach.

Each animal was examined for 4-10 months (5-7 months average).

EXPERIMENTAL RESULTS

After a section 80-100 cm long of the caudal section of the small intestine had been denervated, anemia with a typical intermittent course developed in the cats. The first weeks after denervation, the anemia followed a hypochromic course and was attended by increased reticulocytosis with a shift to the left (Fig. 1). The changes in osmotic fragility and average erythrocyte diameter suggest that anemization is associated with some intensification of hemolysis.

A few "anemic waves", which could be classified as normochromic, normocytic regenerative anemia, usually occurred after the postoperative anemia. There were no signs of intensified blood hemolysis at that time (see Fig. 1). Therefore, denervation of the caudal region of the small intestine causes definite disturbances in the blood system. The functional disturbance of the denervated intestinal section is probably not of

great importance in this context, since, in experiments in which this section of the intestine was resected, only a slight, temporary (3-4 weeks), hypochromic anemia was observed to develop.

Therefore, denervation caused greater change in the blood composition than did resection of the same intestinal section.

More substantial changes were observed in the blood and bone marrow after denervation of the duodenum.

In this case, the anemia was also intermittent in character. During the first period, the number of erythrocytes decreased by 2 million (Fig. 2), and the hemoglobin percentage was reduced at the same time. The anemia was hypochromic. The amount of reticulocytes greatly increased, erythrocyte osmotic fragility changed and microspherocytosis appeared. Erythropoiesis was noticeably intensified (Table 1), which indicates intensified hemolysis. During the second anemic wave, which was classified as hyperchromic, macrocytic and hyporegenerative, a further reduction in the number of erythrocytes occurred. The color index rose above 1. The number of reticulocytes decreased; erythropoiesis was suppressed (see Fig. 2, Table 1). There were no signs of intensified blood hemolysis.

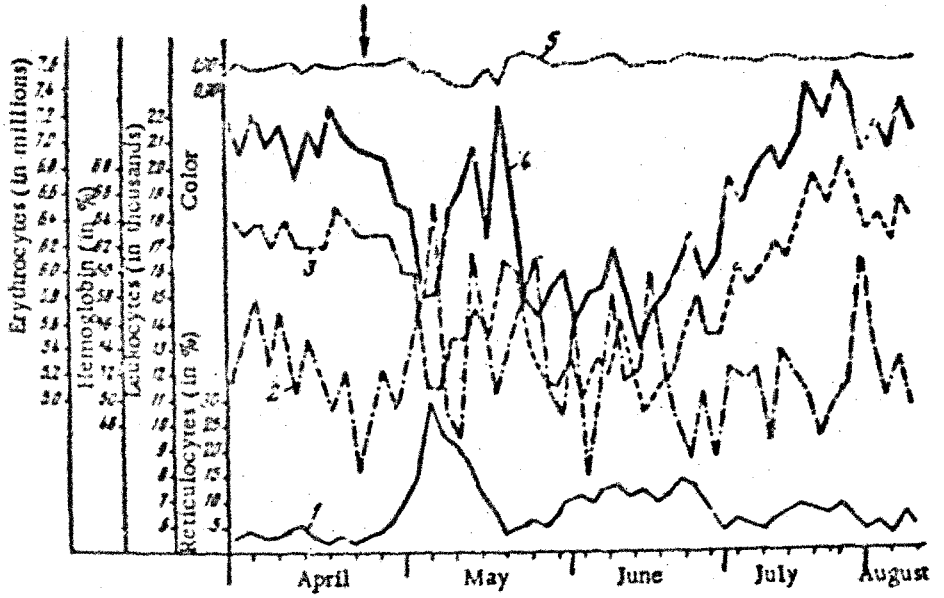

Fig. 1. Change in peripheral blood after denervation of the caudal region of the small intestine.
1) reticulocytes; 2) leukocytes; 3) hemoglobin (according to Sahli); 4) erythrocytes; 5) color index; arrow shows the day of the operation.

Therefore, denervation of the duodenum led to considerable and lasting charges in the blood composition and to erythropoiesis suppression.

It could be suggested that the destruction of the efferent links when the duodenum is denervated could cause the synthesis of the antianemic factor in the mucous membrane of the duodenum to be disturbed. This, however, is not sufficient explanation for the development of such considerable changes in the blood, since the antianemic activity of the duodenum is 3 times less than that of the stomach or of the rest of the intestine.

In the control animals (preparation of the vessels and nerves of the duodenum), a slight, tempory (3-4 weeks) anemia, with some intensification of hemolysis, was observed.

Anemia with the typical intermittent course also developed when the abdominal section of the dogs with a pouch according to Klementsievich and Heidenhain) was denervated.

During the first period, the amount of erythrocytes and hemoglobin sharply decreased, and the reticulocytes

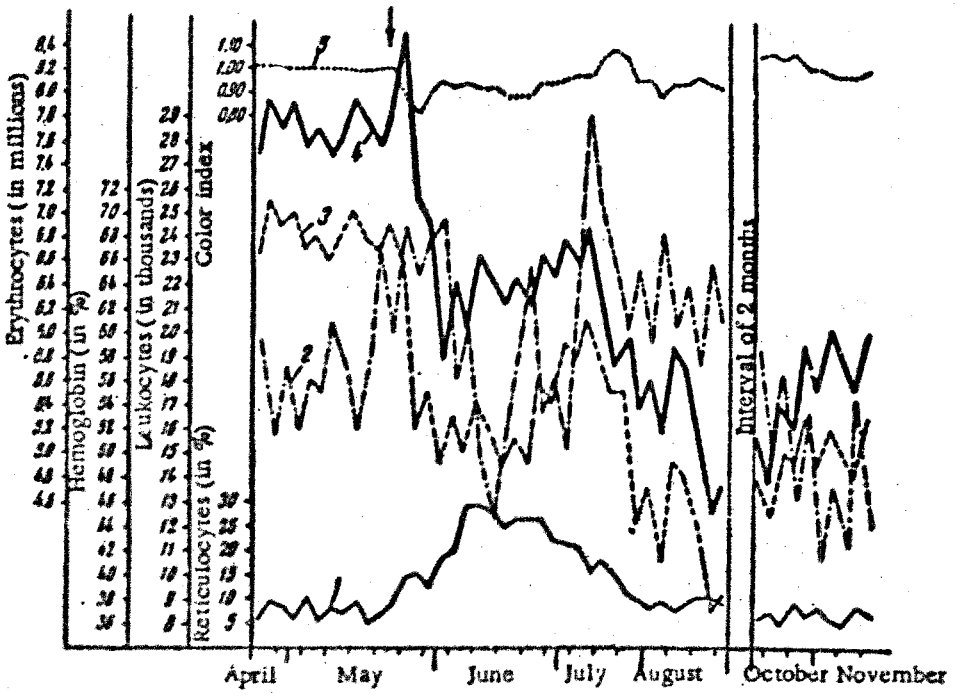

Fig. 2. Change in peripheral blood after denervation of the duodenum. Symbols are the same as in Fig. 1.

TABLE 1

Change in Erythrogenic Portion of Bone Marrow after Denervation of the Duodenum in Cats (in percent of 100 bone marrow cells)

Cat	Date of examination	Period of examination	Amount of dividing forms (mitoses)	Erythroblasts	Proerythroblasts	Normoblasts: Basophilic	Normoblasts: Polychromatophilic	Normoblasts: Orthochromatic	Reticulocytes	Number of erythrocytes per 1 cu mm peripheral blood (in thousands)
№ 18	14/V	Before operation	0.3	0.6	1.1	5.1	11.3	15 7	0.9	7 660
	4/VIII	After operation	0.2	1.0	1.3	5.7	9.6	13.1	1.0	5 190
	28/XI		—	1.3	1.9	4.2	8.1	9.0	0.6	6 000
№ 17	18/V	Before operation	0.2	0.7	1.4	6.3	13.4	17.0	1.1	7 980
	12/VIII	After operation	—	1.2	1.9	4.5	10 0	10.8	0.6	5 840
№ 20	7/V	Before operation	0.4	0.7	1.3	5.8	13.7	16.9	0.9	7 240
	8/VIII	After operation	—	1.3	2.2	3.6	11.2	11.7	0.6	5 710

increased to 5 times the original number (Fig. 3). Also, change in fragility was observed, the average diameter decreased and microspherocytosis appeared. The amount of bilirubin and easily-liberated iron increased. Digestive tract absorption and erythrocyte assimilation of Fe^{59} increased considerably. However, Fe^{59} quickly disappeared from the erythrocytes.

All these signs point to increased hemolysis of the blood.

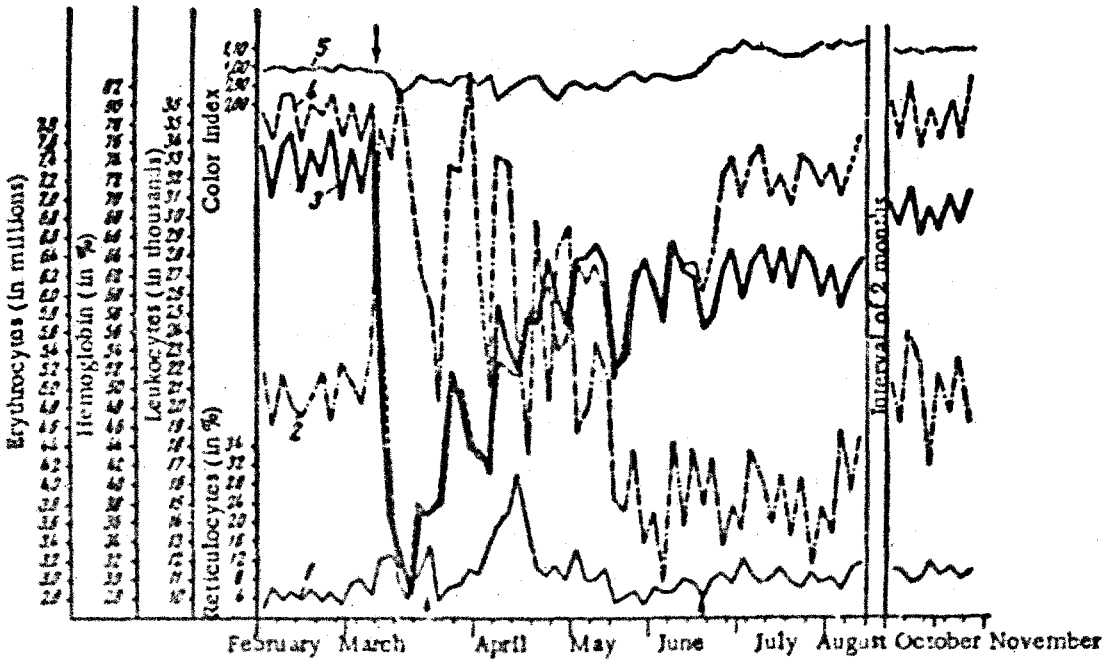

Fig. 3. Change in peripheral blood picture after formation of a pouch in dog Merry according to Klementsievich-Heidenhain. The arrows show radioactive iron administration. The other symbols are the same as in Fig. 1.

The postoperative anemia (Table 2) was classified as the hypochromic, microcytic and regenerative type.

Two months after the operation, the amount of hemoglobin and erythrocytes had increased, but had not yet regained the original level. The erythrocyte deficiency was 1-1,5 millions, which was retained throughout the observation period. The color index rose above 1. The amount of reticulocytes decreased (Fig. 3). Osmotic fragility returned to the original level, and macroplanocytosis appeared. The amount of bilirubin decreased, and the iron again appeared in abundance. The intensity of Fe^{59} absorption and assimilation became almost normal, and the duration of erythrocyte life increased. Erythropoiesis was noticeably suppressed (Table 2).

TABLE 2

Change in Erythrogenic Portion of Bone Marrow after Formation of a Pouch According to Klementsievich-Heidenhain in the dog Merry (in per cent of 100 bone marrow cells)

Examination period	Date of examination	Amount of division forms (mitoses)	Erythroblasts	Pronormoblasts	Normoblasts			Reticulocytes	Number of erythrocytes per 1 cu mm of peripheral blood (1000s)
					Basophilic	Polychromatophilic	Orthochromatic		
Before operation	26/II	0.3	0.6	1.2	6.1	9.2	13.4	0.9	7720
After formation of miniature stomach	23/III	0.4	0.8	1.4	6.7	9.1	13.0	1.8	3830
	22/IV	0.3	0.7	1.4	6.6	9.7	14.2	1.1	5340
	29/VI	0.2	0.9	1.5	7.2	10.8	11.1	0.8	6440
	13/VII	0.1	0.8	1.7	7.9	11.3	10.0	1.2	6320
	10/XI	—	0.8	1.6	8.3	11.8	8.3	1.1	6950

Therefore the anemia was already the hyperchromic, macrocytic, hyporegenerative type.

Consequently, in the long run, denervating a portion of the stomach caused erythropoiesis suppression, which reduced the antianemic activity of the juice from the pouch [9, 11].

However, the pouch was excluded from the digestive processes and did not participate in vitamin B_{12} assimilation; therefore the disturbance of the antianemic factor synthesis in the pouch could not lead to erythropoiesis disturbances. Moreover, in the dogs the pyloric portion of the stomach had a larger antianemic activity than the fundal and, finally, the intestine had a considerable antianemic activity.

Postoperative, hypochromic anemia, characterized by some signs of blood hemolysis intensification, developed in the control dog with a Pavlov pouch. After a month, the blood picture returned to normal.

Postoperative, hypochromic anemia, caused by increased hemolysis, was observed to develop after all our operations, regardless of their nature or localization.

DISCUSSION OF RESULTS

Therefore, denervating various sections of the digestive tract leads to the development of anemias, distinguished by known features. To understand the mechanism of such anemias, one must keep in mind that their first period was characterized by the more or less general traits typical of the anemias which attended the control operations. Evidently, during the first period, the anemias do not have specific features and are an after-effect of operational trauma. It is possible that denervation anemia has a dual mechanism: it is formed from the reaction of the body to the loss of blood and from the reaction to the nervous system trauma caused by the transection of many nerve trunks. In the first period, the anemias are classified as hemolytic.

Then, in the subsequent period, the anemia acquires the specific features described above.

How is it possible, proceeding from factual data, to describe the mechanism of these anemias? They cannot be associated with the decreased function of a given organ or a part of same, since the removal of the spleen or the resection of part of the intestine do not cause anemia like that observed after denervation.

The best way of describing the mechanism of the anemias observed is that they result from the simultaneous blocking of both the afferent and efferent links. The exclusion of these links and others cause the organ, or a section of it, to leave the control of the nervous system; the sections of the central nervous system do not receive the necessary signaling from the periphery and cannot change the organ's operation in the required direction, due to the sectioning of the efferent nerves.

This explanation is based on the theory expressed by V. N. Chernigovsky and A. Ya. Yaroshevsky [10] that the stability of the blood composition is maintained by the constant tonic impulses going from the organs to the central nervous system. The tonic impulses, in their turn, are necessary to realize the efferent, regulating action of the nervous system on the hematopoietic apparatus. Recently, E. Komla published a monograph [13] introducing the view that, in the organs which have to do with hematopoiesis, constant formation of the special substances "poietins" occurs and these substances maintain the normal level of hematopoiesis. Denervation of these organs stops the formation of these substances.

Such an explanation does not negate, but rather supports the thought that the nervous system is probably important to the maintainance of normal activity in the blood system organs. Evidently, "poietins" are only the intermediate humoral link in nervous system regulation of the blood system.

SUMMARY

Studies of the blood picture and bone marrow before and after denervation of various parts of the alimentary canal in animals in series experiments showed that denervation of the caudal part of the small intestine caused the development of a normochromic normocytic anemia; denervation of the duodenum—hyperchromic macrocytic anemia, and denervation of a part of the stomach led to hyperchromic macrocytic anemia.

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